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PASSWORD:
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 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2          "Ask CAS" for self-help around the clock
 NEWS  3  SEP 09  CA/CAplus records now contain indexing from 1907 to the
                  present
 NEWS  4  DEC 08  INPADOC: Legal Status data reloaded
 NEWS  5  SEP 29  DISSABS now available on STN
 NEWS  6  OCT 10  PCTFULL: Two new display fields added
 NEWS  7  OCT 21  BIOSIS file reloaded and enhanced
 NEWS  8  OCT 28  BIOSIS file segment of TOXCENTER reloaded and enhanced
 NEWS  9  NOV 24  MSDS-CCOHS file reloaded
 NEWS 10  DEC 08  CABA reloaded with left truncation
 NEWS 11  DEC 08  IMS file names changed
 NEWS 12  DEC 09  Experimental property data collected by CAS now available
                  in REGISTRY
 NEWS 13  DEC 09  STN Entry Date available for display in REGISTRY and CA/CAplus
 NEWS 14  DEC 17  DGENE: Two new display fields added
 NEWS 15  DEC 18  BIOTECHNO no longer updated
 NEWS 16  DEC 19  CROPU no longer updated; subscriber discount no longer
                  available
 NEWS 17  DEC 22  Additional INPI reactions and pre-1907 documents added to CAS
                  databases
 NEWS 18  DEC 22  IFIPAT/IFIUDB/IFICDB reloaded with new data and search fields
 NEWS 19  DEC 22  ABI-INFORM now available on STN

 NEWS EXPRESS  DECEMBER 28 CURRENT WINDOWS VERSION IS V7.00, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 23 SEPTEMBER 2003
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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

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=> s enprofylline
L1         1352 ENPROFYLLINE

=> s l1 and retin?
L2           29 L1 AND RETIN?

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3           27 DUP REM L2 (2 DUPLICATES REMOVED)

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L3   ANSWER 1 OF 27  USPATFULL on STN
ACCESSION NUMBER:        2003:300856  USPATFULL
TITLE:                   Use of selective adenosine a1 receptor agonists,
                         antagonists and allosteric enhancers to manipulate
                         angiogenesis
INVENTOR(S):             Linden, Joel, Charlottesville, VA, UNITED STATES
                         Tucker, Amy L., Charlottesville, VA, UNITED STATES
                         Price, Richard, Charlottesville, VA, UNITED STATES
                         Youkey, Rebecca, Charlottesville, VA, UNITED STATES

                              NUMBER       KIND    DATE
                         ---------------- ------ --------
PATENT INFORMATION:      US 2003212082      A1   20031113
APPLICATION INFO.:       US 2003-343587     A1   20030131  (10)
                         WO 2001-US24094         20010801
DOCUMENT TYPE:           Utility
FILE SEGMENT:            APPLICATION
LEGAL REPRESENTATIVE:    Hillary W Hawkins, 1032 East Cary Street, Richmond, VA,
                         23219
NUMBER OF CLAIMS:        21
EXEMPLARY CLAIM:         1
NUMBER OF DRAWINGS:      8 Drawing Page(s)
LINE COUNT:              728
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB     Angiogenesis is manipulated by administration of selective adenosine
       A.sub.1 allosteric enhancers can be administered in an amount effective
       to induce angiogenesis at a desired location for treating conditions in
       which increased angiogenesis is desired, such as stroke, heart disease,
       and peripheral vascular disease. Selective A.sub.1 antagonists can be
       administered in an amount effective to inhibit angiogenesis at a desired
       location for treating conditions in which decreased angiogenesis is
       desired , such as for treating tumors, diabetic   ***retinopathy***   ,
       inflammatory diseases such as rheumatoid arthritis and psoriasis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3   ANSWER 2 OF 27  USPATFULL on STN
ACCESSION NUMBER:        2003:294861  USPATFULL
TITLE:                   8-Heteroaryl xanthine adenosine A2B receptor
                         antagonists
INVENTOR(S):             Baraldi, Pier Giovanni, Ferrara, ITALY
                         Borea, Pier A., Ferrara, ITALY

                              NUMBER       KIND    DATE
                         ---------------- ------ --------
PATENT INFORMATION:      US 2003207879      A1   20031106
APPLICATION INFO.:       US 2003-357865     A1   20030203  (10)

                              NUMBER        DATE
                         ----------------- --------
PRIORITY INFORMATION:    US 2002-353317P    20020201 (60)
DOCUMENT TYPE:           Utility
FILE SEGMENT:            APPLICATION
LEGAL REPRESENTATIVE:    EDWARDS & ANGELL, LLP, P.O. Box 9169, Boston, MA, 02209
NUMBER OF CLAIMS:        59
```

NUMBER OF DRAWINGS: 5 Drawing Page(s)
LINE COUNT: 3535
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates generally to compounds of formula (IA):
(IA) ##STR1##

the preparation thereof, pharmaceutical formulations thereof, and their use in medicine as potent or selective A.sub.2B adenosine receptor antagonists and their uses for treating asthma, autoimmune diseases and ***retinal*** vascular diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 3 OF 27 USPATFULL on STN
ACCESSION NUMBER: 2003:127689 USPATFULL
TITLE: Selective antagonists of A2B adenosine receptors
INVENTOR(S): Biaggioni, Italo O., Nashville, TN, UNITED STATES
Feoktistov, Igor A., Nashville, TN, UNITED STATES
Wells, Jack N., Nashville, TN, UNITED STATES
PATENT ASSIGNEE(S): Vanderbilt University (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003087904	A1	20030508
APPLICATION INFO.:	US 2002-285747	A1	20021101 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2000-648775, filed on 28 Aug 2000, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-151649P	19990831 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: A. Blair Hughes, McDonnell Boehnen Hulbert & Berghoff, 32nd Floor, 300 S. Wacker Drive, Chicago, IL, 60606
NUMBER OF CLAIMS: 21
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Page(s)
LINE COUNT: 635
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A compound of the following formula: ##STR1##

wherein R is an aliphatic or cycloaliphatic amine group or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable salt thereof. The compounds of formula (I) may be used to treat, among other indications, asthma and diarrhea.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 4 OF 27 USPATFULL on STN
ACCESSION NUMBER: 2003:127630 USPATFULL
TITLE: COMPOSITION, FORMULATIONS & METHOD FOR PREVENTION & TREATMENT OF DISEASES AND CONDITIONS ASSOCIATED WITH BRONCHOCONSTRICTION, ALLERGY(IES) & INFLAMMATION
INVENTOR(S): NYCE, JONATHAN W., PRINCETON, NJ, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003087845	A1	20030508
APPLICATION INFO.:	US 1998-93972	A1	19980609 (9)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: VIVIANA AMZEL, PH.D., EpiGenesis Pharmaceuticals, Inc., 7 Clarke Drive, Cranbury, NJ, 05812
NUMBER OF CLAIMS: 107
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Page(s)
LINE COUNT: 3682
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A pharmaceutical composition effective for preventing and alleviating bronchoconstriction, allergy(ies) and/or inflammation comprises a surfactant and a nucleic acid comprising an oligonucleotide anti-sense to an adenosine A1, A2a, A2b or A3 receptor gene, mRNA, flanking regions or regions bridging the intro/exon borders, analogues which bind thymidine but have low adenosine content or exhibit lower or no adenosine receptor agonist activity, combinations thereof,

optionally a carrier and other agents such as therapeutic agents and formulation products known in the art. The composition is formulated for administration by a multiplicity of routes for the prevention or alleviation of diseases and conditions associated with breathing difficulties, impeded and obstructed airways, bronchoconstriction, allergy and/or inflammation. Among the appplications of this technology are the prevention and treatment of diseases and conditions such as asthma, kidney damage or failure, ARDS, pulmonary vasoconstriction, inflammation, allergies, impeded respiration, respiratory distress syndrome, pain, cystic fibrosis, pulmonary hypertension, pulmonary vasoconstriction, emphysema, chronic obstructive pulmonary disease (COPD), and cancers such as leukemias, lymphomas, carcinomas, and the like, e.g. colon cancer, breast cancer, lung cancer, pancreatic cancer, hepatocellular carcinoma, kidney cancer, melanoma, hepatic, lung, breast, and prostate metastases, etc., to counter the renal damage and failure associated with ischemic conditions and the administration of certain drugs and radio active diagnostic and therapeutic agents, as well as a joint therapy with the administration of adenosine and adenosine-like agents in the treatment of arrhythmias such as SVT and in cardiovascular function tests (stress tests). The present agent(s) is (are) also suitable for administration before, during and after other treatments, including radiation, chemotherapy, antibody therapy, phototherapy and cancer, and other types of surgery. Alternatively, the present agent may be effectively administered preventatively, prophylactically or therapeutically, and in conjunction with other therapies, or by itself for conditions without known therapies or as a substitute for therapies that have significant negative side effects.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 5 OF 27 USPATFULL on STN
ACCESSION NUMBER: 2003:85867 USPATFULL
TITLE: Oral delivery formulation
INVENTOR(S): Compton, Bruce Jon, Lexington, MA, UNITED STATES
Solari, Nancy E., West Newton, MA, UNITED STATES
Flangan, Margaret A., Stow, MA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003059471	A1	20030327
APPLICATION INFO.:	US 2001-997277	A1	20011129 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1998-55560, filed on 6 Apr 1998, ABANDONED

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-69501P	19971215 (60)
	US 1998-73867P	19980204 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Stephen J Gaudet, 68H Stiles Road, Salem, NH, 03079
NUMBER OF CLAIMS: 42
EXEMPLARY CLAIM: 1
LINE COUNT: 2950
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Flakes containing drugs and methods for forming and using such flakes are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 6 OF 27 USPATFULL on STN
ACCESSION NUMBER: 2003:285098 USPATFULL
TITLE: Compositions and methods to effect the release profile in the transdermal administration of active agents
INVENTOR(S): Kanios, David, Miami, FL, United States
PATENT ASSIGNEE(S): Noven Pharmaceuticals, Inc., Miami, FL, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6638528	B1	20031028
APPLICATION INFO.:	US 2002-86457		20020301 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2001-765932, filed on 19 Jan 2001, now abandoned

	NUMBER	DATE

PRIORITY INFORMATION: US 2000-177103P 20000120 (60)
DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Page, Thurman K.
ASSISTANT EXAMINER: Joynes, Robert M.
LEGAL REPRESENTATIVE: Kolman, Esq., Jay G.
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Figure(s); 6 Drawing Page(s)
LINE COUNT: 2021
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compositions and methods for the transdermal delivery of active agents up to a period of seven days or more at substantially a zero-order release rate comprising a pharmaceutically acceptable adhesive matrix and a polymeric plastic material that provides a release rate regulating effect on the active agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 7 OF 27 USPATFULL on STN
ACCESSION NUMBER: 2003:129695 USPATFULL
TITLE: Bioadhesive compositions and methods for topical administration of active agents
INVENTOR(S): Mantelle, Juan, Miami, FL, United States
Houze, David, Coconut Grove, FL, United States
Kanios, David, Miami, FL, United States
PATENT ASSIGNEE(S): Noven Pharmaceuticals, Inc., Miami, FL, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6562363	B1	20030513	
APPLICATION INFO.:	US 1998-161312		19980928	(9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-61155P	19970926 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Page, Thurman K.
ASSISTANT EXAMINER: Sheikh, Humera N.
LEGAL REPRESENTATIVE: Foley & Lardner
NUMBER OF CLAIMS: 34
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 2672
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Bioadhesive compositions in a flexible, finite form for topical application to skin or mucous membranes comprising a composition which results from an admixture of at least one PVP polymer, at least one bioadhesive, optionally a pharmaceutically acceptable solvent suitable for use with an active agent, and methods of administering active agents to a subject, are disclosed. The bioadhesive composition can either include an active agent incorporated directly in the composition, or a separate source of an active agent.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 8 OF 27 USPATFULL on STN
ACCESSION NUMBER: 2003:96094 USPATFULL
TITLE: Substituted 8-phenylxanthines useful as antagonists of A2B adenosine receptors
INVENTOR(S): Linden, Joel M., Charlottesville, VA, United States
Jacobson, Kenneth A., Silver Spring, MD, United States
Kim, Yong-Chul, Hoover, AL, United States
PATENT ASSIGNEE(S): University of Virginia Patent Foundation, Charlottesville, VA, United States (U.S. corporation)
National Institutes of Health, Rockville, MD, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6545002	B1	20030408	
APPLICATION INFO.:	US 2000-505504		20000217	(9)

	NUMBER	DATE

PRIORITY INFORMATION: US 1999-136898P 19990601 (60)
US 1999-136900P 19990601 (60)
US 1999-151875P 19990831 (60)
DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Berch, Mark L.
LEGAL REPRESENTATIVE: Schwegman, Lundberg, Woessner & Kluth, P.A.
NUMBER OF CLAIMS: 27
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT: 2923
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides compounds having the formula I: ##STR1##

X is (C.sub.1-C.sub.8)alkylene, (C.sub.2-C.sub.8)alkenylene, (C.sub.2-C.sub.8)alkynylene, wherein one of the carbon atoms in the alkylene, alkenylene or alkynylene groups is optionally replaced with a group having the formula --O--, --N(R.sup.4)C(O)--, --OC(O--, S--, --S(O)--or --SO.sub.2--, or a pharmaceutically acceptable salt thereof and pharmaceutical compositions comprising compounds having the formula I. The compounds of the invention are selective antagonists of A.sub.2B adenosine receptors (ARs). These compounds and compositions are useful as pharmaceutical agents for treatment of diseases that are mediated by A.sub.2B adenosine receptors.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 9 OF 27 USPATFULL on STN
ACCESSION NUMBER: 2002:191154 USPATFULL
TITLE: Diagnostic/therapeutic agents
INVENTOR(S): Klaveness, Jo, Oslo, NORWAY
Rongved, Pal, Oslo, NORWAY
Hogset, Anders, Oslo, NORWAY
Tolleshaug, Helge, Oslo, NORWAY
Cuthbertson, Alan, Oslo, NORWAY
Godal, Aslak, Oslo, NORWAY
Hoff, Lars, Oslo, NORWAY
Gogstad, Geir, Oslo, NORWAY
Bryn, Klaus, Oslo, NORWAY
Naevestad, Anne, Oslo, NORWAY
Lovhaug, Dagfinn, Oslo, NORWAY
Hellebust, Halldis, Oslo, NORWAY
Solbakken, Magne, Oslo, NORWAY
PATENT ASSIGNEE(S): Nycomed Imaging AS (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002102217	A1	20020801
	US 6680047	B2	20040120
APPLICATION INFO.:	US 2001-925715	A1	20010810 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1997-959206, filed on 28 Oct 1997, PATENTED

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1996-22366	19961028
	GB 1996-22369	19961028
	GB 1997-2195	19970204
	GB 1997-8265	19970424
	GB 1997-11837	19970606
	GB 1997-11839	19970606
	US 1997-49263P	19970607 (60)
	US 1997-49264P	19970606 (60)
	US 1997-49266P	19970607 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Richard E. Fichter, BACON & THOMAS, PLLC, Fourth Floor, 625 Slaters Lane, Alexandria, VA, 22314-1176
NUMBER OF CLAIMS: 38
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Page(s)
LINE COUNT: 5190
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Targetable diagnostic and/or therapeutically active agents, e.g. ultrasound contrast agents, comprising a suspension in an aqueous carrier liquid of a reporter comprising gas-containing or gas-generating

binding pairs with a target.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 10 OF 27 USPATFULL on STN
ACCESSION NUMBER: 2002:191152 USPATFULL
TITLE: Diagnostic/therapeutic agents
INVENTOR(S): Klaveness, Jo, Oslo, NORWAY
Rongved, Pal, Oslo, NORWAY
Hogset, Anders, Oslo, NORWAY
Tolleshaug, Helge, Oslo, NORWAY
Naevestad, Anne, Oslo, NORWAY
Hellebust, Halldis, Oslo, NORWAY
Hoff, Lars, Oslo, NORWAY
Cuthbertson, Alan, Oslo, NORWAY
Lovhaug, Dagfinn, Oslo, NORWAY
Solbakken, Magne, Oslo, NORWAY
PATENT ASSIGNEE(S): NYCOMED IMAGING AS (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002102215	A1	20020801
APPLICATION INFO.:	US 2001-765614	A1	20010122 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1997-960054, filed on 29 Oct 1997, PATENTED Continuation-in-part of Ser. No. US 1997-958993, filed on 28 Oct 1997, PATENTED

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1996-22366	19961028
	GB 1996-22367	19961028
	GB 1996-22368	19961028
	GB 1997-699	19970115
	GB 1997-8265	19970424
	GB 1997-11842	19970606
	GB 1997-11846	19970606
	US 1997-49264P	19970606 (60)
	US 1997-49265P	19970606 (60)
	US 1997-49268P	19970607 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BACON & THOMAS, PLLC, 4th Floor, 625 Slaters Lane, Alexandria, VA, 22314-1176
NUMBER OF CLAIMS: 37
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Page(s)
LINE COUNT: 6583
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Targetable diagnostic and/or therapeutically active agents, e.g. ultrasound contrast agents, having reporters comprising gas-filled microbubbles stabilized by monolayers of film-forming surfactants, the reporter being coupled or linked to at least one vector.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 11 OF 27 USPATFULL on STN
ACCESSION NUMBER: 2002:17328 USPATFULL
TITLE: Dha-pharmaceutical agent conjugates of taxanes
INVENTOR(S): Shashoua, Victor, Brookline, MA, UNITED STATES
Swindell, Charles, Merion, PA, UNITED STATES
Webb, Nigel, Bryn Mawr, PA, UNITED STATES
Bradley, Matthews, Layton, PA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002010208	A1	20020124
	US 6602902	B2	20030805
APPLICATION INFO.:	US 2001-846838	A1	20010501 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1998-135291, filed on 17 Aug 1998, ABANDONED Continuation of Ser. No. US 1996-651312, filed on 22 May 1996, GRANTED, Pat. No. US 5795909
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Edward R. Gates, Esq., Wolf, Greenfield & Sacks, P.C., 600 Atlantic Avenue, Boston, MA, 02210

EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 14 Drawing Page(s)
LINE COUNT: 2437
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides conjugates of cis-docosahexaenoic acid and pharmaceutical agents useful in treating noncentral nervous system conditions. Methods for selectively targeting pharmaceutical agents to desired tissues are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 12 OF 27 USPATFULL on STN
ACCESSION NUMBER: 2002:8068 USPATFULL
TITLE: Compositions and methods to effect the release profile in the transdermal administration of active agents
INVENTOR(S): Kanios, David, Miami, FL, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002004065	A1	20020110
APPLICATION INFO.:	US 2001-765932	A1	20010119 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-177103P	20000120 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Noven Pharmaceuticals, Inc., 11960 S.W. 144th Street, Miami, FL, 33186
NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Page(s)
LINE COUNT: 2059
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compositions and methods for the transdermal delivery of active agents up to a period of seven days or more at substantially a zero-order release rate comprising a pharmaceutically acceptable adhesive matrix and a polymeric plastic material that provides a release rate regulating effect on the active agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 13 OF 27 USPATFULL on STN
ACCESSION NUMBER: 2001:90260 USPATFULL
TITLE: Fatty acid-pharmaceutical agent conjugates
INVENTOR(S): Webb, Nigel L., Bryn Mawr, PA, United States
Bradley, Matthews O., Laytonsville, MD, United States
Swindell, Charles S., Merion, PA, United States
Shashoua, Victor E., Brookline, MA, United States

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2001002404	A1	20010531
	US 6576636	B2	20030610
APPLICATION INFO.:	US 2000-730450	A1	20001205 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1996-651428, filed on 22 May 1996, ABANDONED
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Edward R. Gates, Wolf, Greenfield & Sacks, P.C., 600 Atlantic Avenue, Boston, MA, 02210
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 14 Drawing Page(s)
LINE COUNT: 2511
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides conjugates of fatty acids and pharmaceutical agents useful in treating noncentral nervous system conditions. Methods for selectively targeting pharmaceutical agents to desired tissues are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 14 OF 27 USPATFULL on STN
ACCESSION NUMBER: 2001:231041 USPATFULL
TITLE: Targeted diagnostic/therapeutic agents having more than

INVENTOR(S): Klaveness, Jo, Olso, Norway
Rongved, P.ang.l, Olso, Norway
H.o slashed.gset, Anders, Olso, Norway
Tolleshaug, Helge, Olso, Norway
Cuthbertson, Alan, Olso, Norway
Hoff, Lars, Olso, Norway
Bryn, Klaus, Olso, Norway
Hellebust, Halldis, Olso, Norway
Solbakken, Magne, Olso, Norway
PATENT ASSIGNEE(S): Nycomed Imaging AS, Oslo, Norway (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6331289	B1	20011218
APPLICATION INFO.:	US 1997-959206		19971028 (8)

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1996-22366	19961028
	GB 1996-22369	19961028
	GB 1997-2195	19970204
	GB 1997-8265	19970424
	GB 1997-11837	19970606
	GB 1997-11839	19970606
	US 1997-49263P	19970606 (60)
	US 1997-49266P	19970607 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Hartley, Michael G.
LEGAL REPRESENTATIVE: Bacon & Thomas
NUMBER OF CLAIMS: 22
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 4091
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Targetable diagnostic and/or therapeutically active agents, e.g. ultrasound contrast agents, comprising a suspension in an aqueous carrier liquid of a reporter comprising gas-containing or gas-generating material, said agent being capable of forming at least two types of binding pairs with a target.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 15 OF 27 USPATFULL on STN
ACCESSION NUMBER: 2001:116526 USPATFULL
TITLE: Targeted ultrasound contrast agents
INVENTOR(S): Klaveness, Jo, Oslo, Norway
Rongved, P.ang.l, Oslo, Norway
L.o slashed.vhaug, Dagfinn, Oslo, Norway
PATENT ASSIGNEE(S): Nycomed Imaging AS, Oslo, Norway (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6264917	B1	20010724
APPLICATION INFO.:	US 1997-958993		19971028 (8)

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1996-22366	19961028
	GB 1996-22367	19961028
	GB 1996-22368	19961028
	GB 1997-699	19970115
	GB 1997-8265	19970424
	GB 1997-11842	19970606
	GB 1997-11846	19970606
	US 1997-49264P	19970607 (60)
	US 1997-49268P	19970607 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Hartley, Michael G.
LEGAL REPRESENTATIVE: Bacon & Thomas
NUMBER OF CLAIMS: 17
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Figure(s); 2 Drawing Page(s)
LINE COUNT: 5477
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ultrasound contrast agents, having reporters comprising gas-filled microbubbles stabilised by monolayers of film-forming surfactants, the reporter being coupled or linked to at least one vector.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 16 OF 27 USPATFULL on STN

ACCESSION NUMBER:	2001:111808 USPATFULL
TITLE:	Diagnostic/therapeutic agents having microbubbles coupled to one or more vectors
INVENTOR(S):	Klaveness, Jo, Oslo, Norway Rongved, P.ang.l, Oslo, Norway H.o slashed.gset, Anders, Oslo, Norway Tolleshaug, Helge, Oslo, Norway N.ae butted.vestad, Anne, Oslo, Norway Hellebust, Halldis, Oslo, Norway Hoff, Lars, Oslo, Norway Cuthbertson, Alan, Oslo, Norway L.o slashed.vhaug, Dagfinn, Oslo, Norway Solbakken, Magne, Oslo, Norway
PATENT ASSIGNEE(S):	Nycomed Imaging AS, Oslo, Norway (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6261537	B1	20010717
APPLICATION INFO.:	US 1997-960054		19971029 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1997-958993, filed on 28 Oct 1997		

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1996-22366	19961028
	GB 1996-22367	19961028
	GB 1996-22368	19961028
	GB 1997-699	19970115
	GB 1997-8265	19970424
	GB 1997-11842	19970606
	GB 1997-11846	19970606
	US 1997-49264P	19970607 (60)
	US 1997-49265P	19970607 (60)
	US 1997-49268P	19970607 (60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	GRANTED
PRIMARY EXAMINER:	Hartley, Michael G.
LEGAL REPRESENTATIVE:	Bacon & Thomas, Fichter, Richard E.
NUMBER OF CLAIMS:	22
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	2 Drawing Figure(s); 2 Drawing Page(s)
LINE COUNT:	5614

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Targetable diagnostic and/or therapeutically active agents, e.g. ultrasound contrast agents, having reporters comprising gas-filled microbubbles stabilised by monolayers of film-forming surfactants, the reporter being coupled or linked to at least one vector.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 17 OF 27 USPATFULL on STN

ACCESSION NUMBER:	2001:59406 USPATFULL
TITLE:	Solubility parameter based drug delivery system and method for altering drug saturation concentration
INVENTOR(S):	Miranda, Jesus, Miami, FL, United States Sablotsky, Steven, Miami, FL, United States
PATENT ASSIGNEE(S):	Noven Pharmaceuticals, Inc., Miami, FL, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6221383	B1	20010424
APPLICATION INFO.:	US 1999-318121		19990525 (9)
RELATED APPLN. INFO.:	Division of Ser. No. US 1997-907906, filed on 11 Aug 1997 Continuation-in-part of Ser. No. US 1994-178558, filed on 7 Jan 1994, now patented, Pat. No. US 5656286, issued on 12 Aug 1997		

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted

ASSISTANT EXAMINER: Williamson, Michael A.
LEGAL REPRESENTATIVE: Foley & Lardner
NUMBER OF CLAIMS: 4
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 20 Drawing Figure(s); 19 Drawing Page(s)
LINE COUNT: 3035
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A blend of at least two polymers, or at least one polymer and a soluble polyvinylpyrrolidone, in combination with a drug provides a pressure-sensitive adhesive composition for a transdermal drug delivery system in which the drug is delivered from the pressure-sensitive adhesive composition and through dermis when the pressure-sensitive adhesive composition is in contact with human skin. According to the invention, soluble polyvinylpyrrolidone can be used to prevent crystallization of the drug, without affecting the rate of drug delivery from the pressure-sensitive adhesive composition.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 18 OF 27 MEDLINE on STN
ACCESSION NUMBER: 2001700409 MEDLINE
DOCUMENT NUMBER: 21583628 PubMed ID: 11726639
TITLE: Adenosine receptor antagonists and ***retinal*** neovascularization in vivo.
AUTHOR: Mino R P; Spoerri P E; Caballero S; Player D; Belardinelli L; Biaggioni I; Grant M B
CORPORATE SOURCE: Department of Molecular Biology and Genetics, University of Florida, Gainesville, FL 32610-0267, USA.
SOURCE: INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE, (2001 Dec) 42 (13) 3320-4.
Journal code: 7703701. ISSN: 0146-0404.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20011220
Last Updated on STN: 20020216
Entered Medline: 20020115
AB PURPOSE: The role of adenosine receptor (AdoR) antagonists in human ***retinal*** endothelial cell function in vitro has previously been determined. In this study, efficacy of AdoR antagonist administration in reducing ***retinal*** neovascularization was examined in a mouse pup model of oxygen-induced ***retinopathy*** . METHODS: A previously described model of oxygen-induced ***retinal*** neovascularization in newborn mouse pups was used to examine the effect of various AdoR antagonists on neovascularization. The nonselective AdoR antagonist xanthine amine congener (XAC), the A(2A)-selective antagonist ZM241385, the A(2B)-selective antagonists 3-N-propylxanthine (***enprofylline***) and 3-isobutyl-8-pyrrolidinoxanthine (IPDX), and the A(1)-selective antagonist cyclopentyl-1,3-dipropylxanthine (CPX) were used. After the hyperoxia exposure the animals received daily intraperitoneal injections of pharmacologically relevant doses of AdoR antagonists for 5 days. Control animals received vehicle (0.1% dimethyl sulfoxide [DMSO]) alone. The animals were then killed and perfused with fluorescein-dextran. Wholemounts of ***retinas*** from one eye were prepared and examined, whereas the ***retinas*** of the contralateral eye were embedded, sectioned, and stained for counting neovascular nuclei extending beyond the internal limiting membrane into the vitreous. RESULTS: Angiography of wholemount ***retinas*** showed reduction of neovascular tufts in animals treated with selective A(2B) AdoR antagonists. Quantification of the extraretinal neovascular nuclei showed that only animals treated with XAC, ***enprofylline*** , or IPDX showed a significant reduction in ***retinal*** neovascularization. By contrast, neither CPX nor ZM241385 had an effect on neovascularization. CONCLUSIONS: The A(2B)-selective AdoR antagonists inhibited oxygen-induced ***retinal*** neovascularization in vivo and may provide a basis for developing pharmacologic therapies for the treatment of proliferative ***retinopathies*** .

L3 ANSWER 19 OF 27 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2001433635 MEDLINE
DOCUMENT NUMBER: 21374019 PubMed ID: 11481274
TITLE: Proliferation, migration, and ERK activation in human ***retinal*** endothelial cells through A(2B) adenosine receptor stimulation.

I; Belardinelli L
CORPORATE SOURCE: Department of Medicine, University of Florida, Gainesville 32610-0267, USA.. grantma@pharmacology.ufl.edu
SOURCE: INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE, (2001 Aug) 42 (9) 2068-73.
Journal code: 7703701. ISSN: 0146-0404.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010820
Last Updated on STN: 20010820
Entered Medline: 20010816

AB PURPOSE: The nucleoside adenosine has been implicated in angiogenesis. A previous study demonstrated that activation of the A(2B) adenosine receptor (AdoR) increases cAMP accumulation, cell proliferation, and VEGF expression in human ***retinal*** endothelial cells (HRECs). In the present study, the role of this receptor was further characterized by examination of the effects of the selective A(2B) AdoR antagonists 3-N-propylxanthine (***enprofylline***) and 3-isobutyl-8-pyrrolidinoxanthine (IPDX) on AdoR-mediated HREC proliferation, capillary tube formation, and signal-transduction pathways. METHODS: HRECs were exposed to the adenosine analogue 5'-N-ethylcarboxamido-adenosine (NECA) in the absence or presence of AdoR antagonists. Migration was measured using Boyden chambers. Proliferation was assessed by counting cells. Western analysis was used to assess extracellular signal-related kinase (ERK) and cAMP response element-binding protein (CREB) in cell lysates. The effect of AdoR activation on tube formation was studied using cells grown on a synthetic basement membrane matrix. RESULTS: NECA induced proliferation in a concentration-dependent manner that was inhibited by ***enprofylline*** and IPDX. NECA stimulated chemotaxis in a concentration-dependent manner that was also blocked by both A(2B) AdoR antagonists. NECA activated ERK and CREB in HRECs. Both A(2B) AdoR antagonists diminished activation of ERK by NECA exposure. ERK activation was also blocked by the ERK-mitogen-activated protein kinase (MAPK) inhibitor PD98059, but not by the protein kinase A (PKA) inhibitor H-89. CREB activation was blocked by H-89, but not by PD98059, suggesting that ERK activation is independent of PKA. NECA enhanced tube formation on the matrix, whereas both A(2B) AdoR antagonists attenuated this effect. CONCLUSIONS: The selective A(2B) AdoR antagonists, ***enprofylline*** and IPDX, inhibited NECA-stimulated proliferation, ERK activation, cell migration, and capillary tube formation. A(2B) AdoR inhibition may offer a way to inhibit ***retinal*** angiogenesis and provide a novel therapeutic approach to treatment of diseases associated with aberrant neovascularization, such as diabetic ***retinopathy*** and ***retinopathy*** of prematurity.

L3 ANSWER 20 OF 27 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:321152 BIOSIS
DOCUMENT NUMBER: PREV200100321152
TITLE: A2B adenosine receptor mediates proliferation, migration, and activation of ERK in human ***retinal*** endothelial cells.
AUTHOR(S): Caballero, S. [Reprint author]; Davis, M. I. [Reprint author]; Grant, M. B. [Reprint author]
CORPORATE SOURCE: Pharmacology and Therapeutics, University of Florida, Gainesville, FL, USA
SOURCE: IOVS, (March 15, 2001) Vol. 42, No. 4, pp. S244. print.
Meeting Info.: Annual Meeting of the Association for Research in Vision and Ophthalmology. Fort Lauderdale, Florida, USA. April 29-May 04, 2001.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 4 Jul 2001
Last Updated on STN: 19 Feb 2002

L3 ANSWER 21 OF 27 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:451406 BIOSIS
DOCUMENT NUMBER: PREV200100451406
TITLE: Proliferation, migration, and signal transduction in human ***retinal*** endothelial cells mediated by the A2B adenosine receptor.
AUTHOR(S): Grant, Maria B. [Reprint author]; Davis, Margaret I. [Reprint author]; Caballero, Sergio [Reprint author]

OURCE: Diabetes, (June, 2001) Vol. 50, No. Supplement 2, pp. A18. print.
Meeting Info.: 61st Scientific Sessions of the American Diabetes Association. Philadelphia, Pennsylvania, USA. June 22-26, 2001. American Diabetes Association.
CODEN: DIAEAZ. ISSN: 0012-1797.
OCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
ANGUAGE: English
NTRY DATE: Entered STN: 19 Sep 2001
Last Updated on STN: 22 Feb 2002

3 ANSWER 22 OF 27 USPATFULL on STN
CCESSION NUMBER: 2000:57775 USPATFULL
ITLE: Method for improving insulin sensitivity using an adenosine receptor antagonist
NVENTOR(S): LaNoue, Kathryn F., Hershey, PA, United States
Crist, George H., Harrisburg, PA, United States
Linden, Joel M., Charlottesville, VA, United States
ATENT ASSIGNEE(S): The Penn State Research Foundation, University Park, PA, United States (U.S. corporation)

	NUMBER	KIND	DATE
ATENT INFORMATION:	US 6060481		20000509
PPLICATION INFO.:	US 1999-259201		19990301 (9)

ELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1998-86101, filed on 28 May 1998, now abandoned
OCUMENT TYPE: Utility
ILE SEGMENT: Granted
RIMARY EXAMINER: Reamer, James H.
EGAL REPRESENTATIVE: Monahan, Thomas J.
UMBER OF CLAIMS: 15
XEMPLARY CLAIM: 1
UMBER OF DRAWINGS: 10 Drawing Figure(s); 10 Drawing Page(s)
INE COUNT: 1277
AS INDEXING IS AVAILABLE FOR THIS PATENT.
B Methods for improving insulin sensitivity in a patient using one or more A.sub.2B adenosine receptor antagonists are disclosed. These methods stimulate insulin dependent glucose uptake in muscle.

AS INDEXING IS AVAILABLE FOR THIS PATENT.

3 ANSWER 23 OF 27 USPATFULL on STN
CCESSION NUMBER: 2000:18064 USPATFULL
ITLE: Solubility parameter based drug delivery system and method for altering drug saturation concentration
NVENTOR(S): Miranda, Jesus, Miami, FL, United States
Sablotsky, Steven, Miami, FL, United States
ATENT ASSIGNEE(S): Noven Pharmaceuticals, Inc., Miami, FL, United States (U.S. corporation)

	NUMBER	KIND	DATE
ATENT INFORMATION:	US 6024976		20000215
PPLICATION INFO.:	US 1997-907906		19970811 (8)

ELATED APPLN. INFO.: Continuation of Ser. No. US 1994-178558, filed on 7 Jan 1994, now patented, Pat. No. US 5656286 which is a continuation-in-part of Ser. No. US 1991-722342, filed on 27 Jun 1991 which is a continuation-in-part of Ser. No. US 671709
OCUMENT TYPE: Utility
ILE SEGMENT: Granted
RIMARY EXAMINER: Venkat, Jyothsna
EGAL REPRESENTATIVE: Foley & Lardner
UMBER OF CLAIMS: 66
XEMPLARY CLAIM: 1
UMBER OF DRAWINGS: 20 Drawing Figure(s); 19 Drawing Page(s)
INE COUNT: 3328
AS INDEXING IS AVAILABLE FOR THIS PATENT.
B A blend of at least two polymers, or at least one polymer and a soluble polyvinylpyrrolidone, in combination with a drug provides a pressure-sensitive adhesive composition for a transdermal drug delivery system in which the drug is delivered from the pressure-sensitive adhesive composition and through dermis when the pressure-sensitive adhesive composition is in contact with human skin. According to the

crystallization of the drug, without affecting the rate of drug delivery from the pressure-sensitive adhesive composition.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 24 OF 27 USPATFULL on STN

ACCESSION NUMBER:	1998:98932 USPATFULL
TITLE:	DHA-pharmaceutical agent conjugates of taxanes
INVENTOR(S):	Shashoua, Victor E., Brookline, MA, United States Swindell, Charles S., Merion, PA, United States Webb, Nigel L., Bryn Mawr, PA, United States Bradley, Matthews O., Laytonsville, MD, United States
PATENT ASSIGNEE(S):	Neuromedica, Inc., Conshohocken, PA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5795909		19980818	
APPLICATION INFO.:	US 1996-651312		19960522	(8)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Jarvis, William R. A.
LEGAL REPRESENTATIVE:	Wolf, Greenfield & Sacks, P.C.
NUMBER OF CLAIMS:	12
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	27 Drawing Figure(s); 14 Drawing Page(s)
LINE COUNT:	2451

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention provides conjugates of cis-docosahexaenoic acid and taxanes useful in treating cell proliferative disorders. Conjugates of paclitaxel and docetaxel are preferred.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 25 OF 27 USPATFULL on STN

ACCESSION NUMBER:	1998:17360 USPATFULL
TITLE:	Compositions and methods for topical administration of pharmaceutically active agents
INVENTOR(S):	Kanios, David P., Miami, FL, United States Gentile, Joseph A., Plantation, FL, United States Mantelle, Juan A., Miami, FL, United States Sablotsky, Steven, Miami, FL, United States
PATENT ASSIGNEE(S):	Noven Pharmaceuticals, Inc., Miami, FL, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5719197		19980217	
APPLICATION INFO.:	US 1995-477361		19950607	(8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1993-112330, filed on 27 Aug 1993, now patented, Pat. No. US 5446070 which is a continuation-in-part of Ser. No. US 1991-813196, filed on 23 Dec 1991, now patented, Pat. No. US 5234957 which is a continuation-in-part of Ser. No. US 1991-661827, filed on 27 Feb 1991, now abandoned , said Ser. No. US 1995-477361, filed on 7 Jun 1995 which is a continuation-in-part of Ser. No. US 1993-67001, filed on 26 May 1993 which is a continuation of Ser. No. US 1991-671709, filed on 2 Apr 1991, now patented, Pat. No. US 5300291 which is a continuation-in-part of Ser. No. US 1989-295847, filed on 11 Jan 1989, now patented, Pat. No. US 4994267 which is a continuation-in-part of Ser. No. US 1988-164482, filed on 4 Mar 1988, now patented, Pat. No. US 4814168			

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Azpuru, Carlos A.
LEGAL REPRESENTATIVE:	Foley & Lardner
NUMBER OF CLAIMS:	27
EXEMPLARY CLAIM:	1
LINE COUNT:	1799

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compositions for topical application comprising a therapeutically effective amount of a pharmaceutical agent(s), a pharmaceutically acceptable bioadhesive carrier, a solvent for the pharmaceutical agent(s) in the carrier and a clay, and methods of administering the

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 26 OF 27 USPATFULL on STN
ACCESSION NUMBER: 97:70731 USPATFULL
TITLE: Solubility parameter based drug delivery system and method for altering drug saturation concentration
INVENTOR(S): Miranda, Jesus, Miami, FL, United States
Sablotsky, Steven, Miami, FL, United States
PATENT ASSIGNEE(S): Noven Pharmaceuticals, Inc., Miami, FL, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5656286		19970812
APPLICATION INFO.:	US 1994-178558		19940107 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1991-722342, filed on 27 Jun 1991, now patented, Pat. No. US 5474783 which is a continuation-in-part of Ser. No. US 1991-671709, filed on 2 Apr 1991, now patented, Pat. No. US 5300291 which is a continuation-in-part of Ser. No. US 1989-295847, filed on 11 Jan 1989, now patented, Pat. No. US 4994267, issued on 19 Feb 1991 which is a continuation-in-part of Ser. No. US 1988-164482, filed on 4 Mar 1988, now patented, Pat. No. US 4814168, issued on 21 Mar 1989
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Venkat, Jyothsna
LEGAL REPRESENTATIVE: Foley & Lardner
NUMBER OF CLAIMS: 73
EXEMPLARY CLAIM: 1,4
NUMBER OF DRAWINGS: 20 Drawing Figure(s); 19 Drawing Page(s)
LINE COUNT: 3344
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A blend of at least two polymers, or at least one polymer and a soluble polyvinylpyrrolidone, in combination with a drug provides a pressure-sensitive adhesive composition for a transdermal drug delivery system in which the drug is delivered from the pressure-sensitive adhesive composition and through dermis when the pressure-sensitive adhesive composition is in contact with human skin. According to the invention, soluble polyvinylpyrrolidone can be used to prevent crystallization of the drug, without affecting the rate of drug delivery from the pressure-sensitive adhesive composition.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 27 OF 27 USPATFULL on STN
ACCESSION NUMBER: 95:78209 USPATFULL
TITLE: Compositions and methods for topical administration of pharmaceutically active agents
INVENTOR(S): Mantelle, Juan A., Miami, FL, United States
PATENT ASSIGNEE(S): Nover Pharmaceuticals, Inc., Miami, FL, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5446070		19950829
APPLICATION INFO.:	US 1993-112330		19930827 (8)

DISCLAIMER DATE: 20100810
RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1991-813196, filed on 23 Dec 1991, now patented, Pat. No. US 5234957 which is a continuation-in-part of Ser. No. US 1991-661827, filed on 27 Feb 1991, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Page, Thurman K.
ASSISTANT EXAMINER: Azpuru, Carlos
LEGAL REPRESENTATIVE: Foley & Lardner
NUMBER OF CLAIMS: 45
EXEMPLARY CLAIM: 1
LINE COUNT: 2434
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compositions for topical application comprising a therapeutically effective amount of a pharmaceutical agent(s), a pharmaceutically acceptable carrier, and a solvent for the pharmaceutical agent(s) in the

mammal are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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NEWS	5	SEP 29	DISSABS now available on STN
NEWS	6	OCT 10	PCTFULL: Two new display fields added
NEWS	7	OCT 21	BIOSIS file reloaded and enhanced
NEWS	8	OCT 28	BIOSIS file segment of TOXCENTER reloaded and enhanced
NEWS	9	NOV 24	MSDS-CCOHS file reloaded
NEWS	10	DEC 08	CABA reloaded with left truncation
NEWS	11	DEC 08	IMS file names changed
NEWS	12	DEC 09	Experimental property data collected by CAS now available in REGISTRY
NEWS	13	DEC 09	STN Entry Date available for display in REGISTRY and CA/CAplus
NEWS	14	DEC 17	DGENE: Two new display fields added
NEWS	15	DEC 18	BIOTECHNO no longer updated
NEWS	16	DEC 19	CROPU no longer updated; subscriber discount no longer available
NEWS	17	DEC 22	Additional INPI reactions and pre-1907 documents added to CAS databases
NEWS	18	DEC 22	IFIPAT/IFIUDB/IFICDB reloaded with new data and search fields
NEWS	19	DEC 22	ABI-INFORM now available on STN

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=> s enprofylline and (retina or retinal)
L1 14 ENPROFYLLINE AND (RETINA OR RETINAL)

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PROCESSING COMPLETED FOR L1
L2 12 DUP REM L1 (2 DUPLICATES REMOVED)

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L2 ANSWER 1 OF 12 USPATFULL on STN
ACCESSION NUMBER: 2003:294861 USPATFULL
TITLE: 8-Heteroaryl xanthine adenosine A2B receptor antagonists
INVENTOR(S): Baraldi, Pier Giovanni, Ferrara, ITALY
Borea, Pier A., Ferrara, ITALY

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003207879	A1	20031106
APPLICATION INFO.:	US 2003-357865	A1	20030203 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-353317P	20020201 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: EDWARDS & ANGELL, LLP, P.O. Box 9169, Boston, MA, 02209
NUMBER OF CLAIMS: 59
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Page(s)
LINE COUNT: 3535
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB . . . use in medicine as potent or selective A.sub.2B adenosine receptor antagonists and their uses for treating asthma, autoimmune diseases and ***retinal*** vascular diseases.
SUMM . . . A.sub.2B adenosine receptor antagonist compounds for inhibiting mammalian cell proliferation in cells that express the A.sub.2B adenosine receptor including human ***retinal*** endothelial cells (HREC). Belardinelli discloses such treatment for ischemic injury to ***retinal*** vessels, for example, microvascular abnormalities of the ***retina*** , retinopathy, prematurity, macular degeneration, and diabetic retinopathy. U.S. patent application Ser. No. 2002/0002142 to Belardinelli et al. is incorporated by. . .
SUMM [0007] The use of A.sub.2B antagonists as antiasthmatic agents is supported by the experimental observation that theophylline and ***enprofylline*** are used as therapeutic agents (Feoktistov and

alkyl-xanthine that is a. . .

SUMM [0009] As noted the xanthine derivative, ***enprofylline*** , is also used to treat asthma. ***Enprofylline*** has been reported to block A.sub.2B adenosine receptors. However, this compounds only weakly blocks A.sub.1, A.sub.2A and A.sub.3 adenosine receptors.

SUMM [0010] It has been reported that therapeutic concentrations of theophylline or ***enprofylline*** block human A.sub.2B receptors, and it has been proposed that antagonists selective for this subtype may have potential use as. . . agents. (See Feoktistov et al., Pharmacol. Rev. 1997, 49, 381-402; and Robeva et al., Drug Dev. Res. 1996, 39, 243-252. ***Enprofylline*** has a reported K.sub.i value of 7 .mu.M and is somewhat selective in binding to human A.sub.2B adenosine receptors. (See. . .

SUMM [0012] Both of these xanthine derivatives, ***enprofylline*** and theophylline, are proven to be effective but with low potency and selectivity at the A.sub.2B adenosine receptor subtype (theophylline A.sub.2B binding affinity K.sub.i=13 .mu.M; ***enprofylline*** A.sub.2B binding affinity K.sub.i=7 .mu.M).

SUMM [0052] Similarly, the compounds can be used in a method for the treatment of diseases involving microvascular abnormalities of the ***retina*** that are mediated by adenosine A.sub.2B receptors. Such diseases include, but are not limited to, retinopathy, prematurity, macular degeneration, and. . .

DETD . . . the present invention may be used for inhibiting cell proliferation in cells that express the A.sub.2B adenosine receptor including human ***retinal*** endothelial cells (HREC). Such uses include treatment for chronic and acute inflammatory diseases involving degranulation of mast cells including asthma,. . .

DETD [0410] Similarly, the compounds can be used in a method for the treatment of diseases involving microvascular abnormalities of the ***retina*** that are mediated by adenosine A.sub.2B receptors. Such diseases include, but are not limited to, retinopathy, prematurity, macular degeneration, and. . .

DETD [0430] When used in the treatment of treatment for ischemic injury to ***retinal*** vessels the compounds of the present invention are preferably formulated in eyedrops suitable for topical application.

DETD [0485] Feoktistov I, Biaggioni I. 1995. Adenosine A2B receptors evoke interleukine-S secretion in human mast cells: an ***enprofylline*** -sensitive mechanism with implication for asthma. J. Clin Invest 96: 1979-1986.

CLM What is claimed is:

. . . mediated by adenosine A.sub.2B receptors involves treating of a disorder selected from the group consisting of microvascular abnormalities of the ***retina*** , retinopathy, prematurity, macular degeneration, and diabetic retinopathy.

. . . mediated by adenosine A.sub.2B receptors involves treating of a disorder selected from the group consisting of microvascular abnormalities of the ***retina*** , retinopathy, prematurity, macular degeneration, and diabetic retinopathy.

. . . mediated by adenosine A.sub.2B receptors involves treating of a disorder selected from the group consisting of microvascular abnormalities of the ***retina*** , retinopathy, prematurity, macular degeneration, and diabetic retinopathy.

. . . mediated by adenosine A.sub.2B receptors involves treating of a disorder selected from the group consisting of microvascular abnormalities of the ***retina*** , retinopathy, prematurity, macular degeneration, and diabetic retinopathy.

. . . mediated by adenosine A.sub.2B receptors involves treating of a disorder selected from the group consisting of microvascular abnormalities of the ***retina*** , retinopathy, prematurity, macular degeneration, and diabetic retinopathy.

. . . mediated by adenosine A.sub.2B receptors involves treating of a disorder selected from the group consisting of microvascular abnormalities of the ***retina*** , retinopathy, prematurity, macular degeneration, and diabetic retinopathy.

. . . by adenosine A.sub.2B receptors involves the treating of a disorder selected from the group consisting of microvascular abnormalities of the ***retina*** , retinopathy, prematurity, macular degeneration, and diabetic retinopathy.

disorder selected from the group consisting of microvascular abnormalities of the ***retina*** , retinopathy, prematurity, macular degeneration, and diabetic retinopathy.

. . . mediated by adenosine A.sub.2B receptors involves treating of a disorder selected from the group consisting of microvascular abnormalities of the ***retina*** , retinopathy, prematurity, macular degeneration, and diabetic retinopathy.

L2 ANSWER 2 OF 12 USPATFULL on STN
ACCESSION NUMBER: 2003:85867 USPATFULL
TITLE: Oral delivery formulation
INVENTOR(S): Compton, Bruce Jon, Lexington, MA, UNITED STATES
Solari, Nancy E., West Newton, MA, UNITED STATES
Flangan, Margaret A., Stow, MA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003059471	A1	20030327
APPLICATION INFO.:	US 2001-997277	A1	20011129 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1998-55560, filed on 6 Apr 1998, ABANDONED

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-69501P	19971215 (60)
	US 1998-73867P	19980204 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Stephen J Gaudet, 68H Stiles Road, Salem, NH, 03079
NUMBER OF CLAIMS: 42
EXEMPLARY CLAIM: 1
LINE COUNT: 2950
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . Bronchodilator: Albuterol; Albuterol Sulfate; Azanator Maleate; Bamifylline Hydrochloride; Bitolterol Mesylate; Butaprost; Carbuterol Hydrochloride; Clorprenaline Hydrochloride; Colterol Mesylate; Doxaprost; Doxofylline; Dyphylline; ***Enprofylline*** ; Ephedrine; Ephedrine Hydrochloride; Fenoterol; Fenprinast Hydrochloride; Guaithylline; Hexoprenaline Sulfate; Hoquizil Hydrochloride; Ipratropium Bromide; Isoetharine; Isoetharine Hydrochloride; Isoetharine Mesylate; Isoproterenol Hydrochloride;. . .
SUMM . . . antioxidants useful in the present invention may be selected from the group consisting of all forms of Vitamin A including ***retinal*** and 3,4-didehydroretinal, all forms of carotene such as Alpha-carotene, beta-carotene (beta, beta-carotene), gamma-carotene, delta-carotene, all forms of Vitamin C (D-ascorbic. . .

L2 ANSWER 3 OF 12 USPATFULL on STN
ACCESSION NUMBER: 2002:191154 USPATFULL
TITLE: Diagnostic/therapeutic agents
INVENTOR(S): Klaveness, Jo, Oslo, NORWAY
Rongved, Pal, Oslo, NORWAY
Hogset, Anders, Oslo, NORWAY
Tolleshaug, Helge, Oslo, NORWAY
Cuthbertson, Alan, Oslo, NORWAY
Godal, Aslak, Oslo, NORWAY
Hoff, Lars, Oslo, NORWAY
Gogstad, Geir, Oslo, NORWAY
Bryn, Klaus, Oslo, NORWAY
Naevestad, Anne, Oslo, NORWAY
Lovhaug, Dagfinn, Oslo, NORWAY
Hellebust, Halldis, Oslo, NORWAY
Solbakken, Magne, Oslo, NORWAY
PATENT ASSIGNEE(S): Nycomed Imaging AS (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002102217	A1	20020801
	US 6680047	B2	20040120
APPLICATION INFO.:	US 2001-925715	A1	20010810 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1997-959206, filed on 28 Oct 1997, PATENTED

	NUMBER	DATE

PRIORITY INFORMATION: GB 1996-22366 19961028
GB 1996-22369 19961028
GB 1997-2195 19970204
GB 1997-8265 19970424
GB 1997-11837 19970606
GB 1997-11839 19970606
US 1997-49263P 19970607 (60)
US 1997-49264P 19970606 (60)
US 1997-49266P 19970607 (60)
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Richard E. Fichter, BACON & THOMAS, PLLC, Fourth Floor, 625 Slaters Lane, Alexandria, VA, 22314-1176
NUMBER OF CLAIMS: 38
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Page(s)
LINE COUNT: 5190
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . Monocytes
antibodies macrophages
liver
Transferrin transferrin-receptor Tumours
vessel walls
streptokinase/tissue plasminogen activator thrombi thrombi
Plasminogen, plasmin Fibrin Thrombi, tumours
Mast cell proteoglycans
proteinases
Elastase proteoglycans
Lipoprotein lipase proteoglycans
Coagulation enzymes proteoglycans
Extracellular superoxide dismutase proteoglycans
Heparin cofactor II proteoglycans
Retinal survival factor specific receptors proteoglycans
Heparin-binding brain mitogen proteoglycans
Apolipoprotein, e.g. apolipoprotein B specific receptors (e.g., LDL receptor) proteoglycans
Apolipoprotein E LDL receptor proteoglycans
Adhesion-promoting proteins, e.g.. . . proteoglycans
SUMM . . . endralazine, endrysone, enefexine, enestebol, enfenamic acid, enflurane, eniclobrate, enilconazole, enilospirone, enisoprost, enocitabine, enolicam, enoxacin, enoxamast, enoximone, enoxolone, eniprazole, eniproline, enprazepine, ***enprofylline*** , enpromate, enprostil, enrofloxacin, entsufon sodium, enviomycin, enviradene, epalretat, epanolol, eperisone, ephedrine, epicainide, epicillin, epicriptine, epiestriol, epimestrol, epinastine, epinephrine, epinephryl borate,. . .

L2 ANSWER 4 OF 12 USPATFULL on STN
ACCESSION NUMBER: 2002:191152 USPATFULL
TITLE: Diagnostic/therapeutic agents
INVENTOR(S): Klaveness, Jo, Oslo, NORWAY
Rongved, Pal, Oslo, NORWAY
Hogset, Anders, Oslo, NORWAY
Tolleshaug, Helge, Oslo, NORWAY
Naevestad, Anne, Oslo, NORWAY
Hellebust, Halldis, Oslo, NORWAY

Cuthbertson, Alan, Oslo, NORWAY
Lovhaug, Dagfinn, Oslo, NORWAY
Solbakken, Magne, Oslo, NORWAY
PATENT ASSIGNEE(S): NYCOMED IMAGING AS (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002102215	A1	20020801
APPLICATION INFO.:	US 2001-765614	A1	20010122 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1997-960054, filed on 29 Oct 1997, PATENTED Continuation-in-part of Ser. No. US 1997-958993, filed on 28 Oct 1997, PATENTED

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1996-22366	19961028
	GB 1996-22367	19961028
	GB 1996-22368	19961028
	GB 1997-699	19970115
	GB 1997-8265	19970424
	GB 1997-11842	19970606
	GB 1997-11846	19970606
	US 1997-49264P	19970606 (60)
	US 1997-49265P	19970606 (60)
	US 1997-49268P	19970607 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BACON & THOMAS, PLLC, 4th Floor, 625 Slaters Lane, Alexandria, VA, 22314-1176
NUMBER OF CLAIMS: 37
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Page(s)
LINE COUNT: 6583
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . walls
Streptokinase/ tissue plasminogen activator — thrombi — thrombi
Plasminogen, plasmin — Fibrin — Thrombi, tumours
Mast cell proteinases — proteoglycans
Elastase — proteoglycans
Lipoprotein lipase — proteoglycans
Coagulation enzymes — proteoglycans
Extracellular superoxide dismutase — proteoglycans
Heparin cofactor II — proteoglycans
Retinal survival factor — proteoglycans
Heparin-binding brain mitogen — proteoglycans
Apolipoprotein, e.g. apolipoprotein B — proteoglycans
Apolipoprotein E — LDL. . .
DETD . . . endralazine, endrysone, enefexine, enestebol, enfenamic acid,

enocitabine, enolicam, enoxacin, enoxamast, enoximone, enoxolone, eniprazole, eniproline, enprazepine, ***enprofylline*** , enpromate, enprostil, enrofloxacin, entsufon sodium, enviomycin, enviradene, epalretat, epanolol, eperisone, ephedrine, epicainide, epicillin, epicriptine, epiestriol, epimestrol, epinastine, epinephrine, epinephryl borate,. . .

L2 ANSWER 5 OF 12 USPATFULL on STN

ACCESSION NUMBER:	2001:231041 USPATFULL
TITLE:	Targeted diagnostic/therapeutic agents having more than one different vectors
INVENTOR(S):	Klaveness, Jo, Olso, Norway Rongved, P.ang.l, Olso, Norway H.o slashed.gset, Anders, Olso, Norway Tolleshaug, Helge, Olso, Norway Cuthbertson, Alan, Olso, Norway Hoff, Lars, Olso, Norway Bryn, Klaus, Olso, Norway Hellebust, Halldis, Olso, Norway Solbakken, Magne, Olso, Norway
PATENT ASSIGNEE(S):	Nycomed Imaging AS, Oslo, Norway (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6331289	B1	20011218	
APPLICATION INFO.:	US 1997-959206		19971028	(8)

	NUMBER	DATE	
PRIORITY INFORMATION:	GB 1996-22366	19961028	
	GB 1996-22369	19961028	
	GB 1997-2195	19970204	
	GB 1997-8265	19970424	
	GB 1997-11837	19970606	
	GB 1997-11839	19970606	
	US 1997-49263P	19970606	(60)
	US 1997-49266P	19970607	(60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	GRANTED
PRIMARY EXAMINER:	Hartley, Michael G.
LEGAL REPRESENTATIVE:	Bacon & Thomas
NUMBER OF CLAIMS:	22
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT:	4091

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . Monocytes		
antibodies		macrophages liver
Transferrin	transferrin- receptor	Tumours vessel walls
Streptokinase/ tissue plasminogen activator	thrombi	thrombi
Plasminogen, plasmin	Fibrin	Thrombi, tumours
Mast cell proteinases	proteoglycans	
Elastase	proteoglycans	
Lipoprotein lipase	proteoglycans	
Coagulation enzymes	proteoglycans	
Extracellular superoxide dismutase	proteoglycans	
Heparin cofactor II	proteoglycans	
Retinal factor	survival specific receptors	proteoglycans
Heparin-binding brain mitogen	proteoglycans specific receptors	
Apolipoprotein,	proteoglycans	

polipoprotein B receptors
(e.g., LDL
receptor)
polipoprotein E LDL receptor
proteoglycans
dhesion- proteoglycans
romoting
roteins,
.g.. . .
ETD . . . endralazine, endrysone, enefexine, enestebol, enfenamic acid, enflurane, eniclobrate, enilconazole, enilospirone, enisoprost, enocitabine, enolicam, enoxacin, enoxamast, enoximone, enoxolone, eniprazole, eniproline, enprazepine, ***enprofylline*** , enpromate, enprostil, enrofloxacin, entsufon sodium, enviomycin, enviradene, epalretat, epanolol, eperisone, ephedrine, epicainide, epicillin, epicriptine, epiestriol, epimestrol, epinastine, epinephrine, epinephryl borate,. . .

2 ANSWER 6 OF 12 USPATFULL on STN
CCESSION NUMBER: 2001:116526 USPATFULL
ITLE: Targeted ultrasound contrast agents
NVENTOR(S): Klaveness, Jo, Oslo, Norway
Rongved, P.ang.l, Oslo, Norway
L.o slashed.vhaug, Dagfinn, Oslo, Norway
ATENT ASSIGNEE(S): Nycomed Imaging AS, Oslo, Norway (non-U.S. corporation)

	NUMBER	KIND	DATE	
ATENT INFORMATION:	US 6264917	B1	20010724	
PPLICATION INFO.:	US 1997-958993		19971028	(8)

	NUMBER	DATE	
RIORITY INFORMATION:	GB 1996-22366	19961028	
	GB 1996-22367	19961028	
	GB 1996-22368	19961028	
	GB 1997-699	19970115	
	GB 1997-8265	19970424	
	GB 1997-11842	19970606	
	GB 1997-11846	19970606	
	US 1997-49264P	19970607	(60)
	US 1997-49268P	19970607	(60)

OCUMENT TYPE: Utility
ILE SEGMENT: GRANTED
RIMARY EXAMINER: Hartley, Michael G.
EGAL REPRESENTATIVE: Bacon & Thomas
UMBER OF CLAIMS: 17
XEMPLARY CLAIM: 1
UMBER OF DRAWINGS: 2 Drawing Figure(s); 2 Drawing Page(s)
INE COUNT: 5477
AS INDEXING IS AVAILABLE FOR THIS PATENT.
ETD . . . walls
treptokinase/ thrombi thrombi
issue
lasminogen
ctivator
lasminogen, Fibrin Thrombi, 32
lasmin tumours
ast cell proteoglycans 33
roteinases
lastase proteoglycans 34
ipoprotein proteoglycans 35
ipase
oagulation proteoglycans 36
nzymes
xtracellular proteoglycans 37
uperoxide
ismutase
eparin cofactor proteoglycans 38
I
Retinal survival proteoglycans 39
actor specific
receptors
eparin-binding proteoglycans 40
rain mitogen specific
receptors

e.g. specific
apolipoprotein B receptors
(e.g., LDL
receptor)
Apolipoprotein E LDL. . .
DETD . . . endralazine, endrysone, enefexine, enestebol, enfenamic acid,
enflurane, eniclobrate, enilconazole, enilospirone, enisoprost,
enocitabine, enolicam, enoxacin, enoxamast, enoximone, enoxolone,
eniprazole, eniproline, enprazepine, ***enprofylline*** , enpromate,
enprostil, enrofloxacin, entsufon sodium, enviomycin, enviradene,
epalretat, epanolol, eperisone, ephedrine, epicainide, epicillin,
epicriptine, epiestriol, epimestrol, epinastine, epinephrine, epinephryl
borate,. . .

L2 ANSWER 7 OF 12 USPATFULL on STN
ACCESSION NUMBER: 2001:111808 USPATFULL
TITLE: Diagnostic/therapeutic agents having microbubbles coupled to one or more vectors
INVENTOR(S): Klaveness, Jo, Oslo, Norway
Rongved, P.ang.l, Oslo, Norway
H.o slashed.gset, Anders, Oslo, Norway
Tolleshaug, Helge, Oslo, Norway
N.ae butted.vestad, Anne, Oslo, Norway
Hellebust, Halldis, Oslo, Norway
Hoff, Lars, Oslo, Norway
Cuthbertson, Alan, Oslo, Norway
L.o slashed.vhaug, Dagfinn, Oslo, Norway
Solbakken, Magne, Oslo, Norway
PATENT ASSIGNEE(S): Nycomed Imaging AS, Oslo, Norway (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6261537	B1	20010717
APPLICATION INFO.:	US 1997-960054		19971029 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1997-958993, filed on 28 Oct 1997

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1996-22366	19961028
	GB 1996-22367	19961028
	GB 1996-22368	19961028
	GB 1997-699	19970115
	GB 1997-8265	19970424
	GB 1997-11842	19970606
	GB 1997-11846	19970606
	US 1997-49264P	19970607 (60)
	US 1997-49265P	19970607 (60)
	US 1997-49268P	19970607 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Hartley, Michael G.
LEGAL REPRESENTATIVE: Bacon & Thomas, Fichter, Richard E.
NUMBER OF CLAIMS: 22
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Figure(s); 2 Drawing Page(s)
LINE COUNT: 5614
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ORWD . . . walls
Streptokinase/ thrombi thrombi
tissue
plasminogen
activator
Plasminogen, Fibrin Thrombi, 32
plasmin tumours
Mast cell proteoglycans 33
proteinases
Elastase proteoglycans 34
Lipoprotein proteoglycans 35
lipase
Coagulation proteoglycans 36
enzymes
Extracellular proteoglycans 37
superoxide
dismutase
Heparin cofactor proteoglycans 38

Retinal survival proteoglycans 39
factor specific
receptors
Heparin-binding proteoglycans 40
brain nitrogen specific
receptors
Apolipoprotein, proteoglycans 41
e.g. specific
apolipoprotein B receptors
(e.g., LDL
receptor)
Apolipoprotein E LDL. . .
ORWD . . . endralazine, endrysone, enefexine, enestebol, enfenamic acid, enflurane, eniclobrate, enilconazole, enilospirone, enisoprost, enocitabine, enolicam, enoxacin, enoxamast, enoximone, enoxolone, eniprazole, eniproline, enprazepine, ***enprofylline*** , enpromate, enprostil, enrofloxacin, entsufon sodium, enviomycin, enviradene, epalretat, epanolol, eperisone, ephedrine, epicainide, epicillin, epicriptine, epiestriol, epimestrol, epinastine, epinephrine, epinephryl borate,. . .

L2 ANSWER 8 OF 12 USPATFULL on STN
ACCESSION NUMBER: 2001:59406 USPATFULL
TITLE: Solubility parameter based drug delivery system and method for altering drug saturation concentration
INVENTOR(S): Miranda, Jesus, Miami, FL, United States
Sablotsky, Steven, Miami, FL, United States
PATENT ASSIGNEE(S): Noven Pharmaceuticals, Inc., Miami, FL, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6221383	B1	20010424
APPLICATION INFO.:	US 1999-318121		19990525 (9)

RELATED APPLN. INFO.: Division of Ser. No. US 1997-907906, filed on 11 Aug 1997 Continuation-in-part of Ser. No. US 1994-178558, filed on 7 Jan 1994, now patented, Pat. No. US 5656286, issued on 12 Aug 1997
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Dodson, Shelley A.
ASSISTANT EXAMINER: Williamson, Michael A.
LEGAL REPRESENTATIVE: Foley & Lardner
NUMBER OF CLAIMS: 4
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 20 Drawing Figure(s); 19 Drawing Page(s)
LINE COUNT: 3035
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD Xanthine derivatives such as Acefylline, Acefylline Piperazine, Ambuphylline, Aminophylline, Bamifylline, choline Theophyllinate, Doxofylline, Dyphylline, ***Enprofylline*** , Etamiphyllin, Etofylline, Guaithylline, Proxyphylline, Theobromine, 1-Theobromineacetic Acid and Theophylline; and
DETD . . . readily soluble in the polymer system, a co-solvent for the drug and polymer can be added. Co-solvents, such as lecithin, ***retinal*** derivatives, tocopherol, dipropylene glycol, triacetin, propylene glycol, saturated and unsaturated fatty acids, mineral oil, silicone fluid, alcohols, butyl benzyl phthalate,. . .

L2 ANSWER 9 OF 12 MEDLINE on STN
ACCESSION NUMBER: 2001700409 MEDLINE
DOCUMENT NUMBER: 21583628 PubMed ID: 11726639
TITLE: Adenosine receptor antagonists and ***retinal*** neovascularization in vivo.
AUTHOR: Mino R P; Spoerri P E; Caballero S; Player D; Belardinelli L; Biaggioni I; Grant M B
CORPORATE SOURCE: Department of Molecular Biology and Genetics, University of Florida, Gainesville, FL 32610-0267, USA.
SOURCE: INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE, (2001 Dec) 42 (13) 3320-4.
Journal code: 7703701. ISSN: 0146-0404.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 200201

Last Updated on STN: 20020216
Entered Medline: 20020115

TI Adenosine receptor antagonists and ***retinal*** neovascularization in vivo.

AB PURPOSE: The role of adenosine receptor (AdoR) antagonists in human ***retinal*** endothelial cell function in vitro has previously been determined. In this study, efficacy of AdoR antagonist administration in reducing ***retinal*** neovascularization was examined in a mouse pup model of oxygen-induced retinopathy. METHODS: A previously described model of oxygen-induced ***retinal*** neovascularization in newborn mouse pups was used to examine the effect of various AdoR antagonists on neovascularization. The nonselective AdoR antagonist xanthine amine congener (XAC), the A(2A)-selective antagonist ZM241385, the A(2B)-selective antagonists 3-N-propylxanthine (***enprofylline***) and 3-isobutyl-8-pyrrolidinoxanthine (IPDX), and the A(1)-selective antagonist cyclopentyl-1,3-dipropylxanthine (CPX) were used. After the hyperoxia exposure the animals received daily intraperitoneal. . . animals treated with selective A(2B) AdoR antagonists. Quantification of the extraretinal neovascular nuclei showed that only animals treated with XAC, ***enprofylline*** , or IPDX showed a significant reduction in ***retinal*** neovascularization. By contrast, neither CPX nor ZM241385 had an effect on neovascularization. CONCLUSIONS: The A(2B)-selective AdoR antagonists inhibited oxygen-induced ***retinal*** neovascularization in vivo and may provide a basis for developing pharmacologic therapies for the treatment of proliferative retinopathies.

CT . . .
Mice
Mice, Inbred C57BL
*Neovascularization, Pathologic: PC, prevention & control
Pyrrolidinones: PD, pharmacology
*Receptors, Purinergic P1: AI, antagonists & inhibitors
*** Retina: DE, drug effects***
*** Retina: PA, pathology***
****Retinal Vessels***
*** Retinal Vessels: RA, radiography***
Xanthines: PD, pharmacology

RN ***41078-02-8 (enprofylline)*** ; 96865-92-8 (8-(4-((2-aminoethyl)aminocarbonylmethyloxy)phenyl)-1,3-dipropylxanthine)

L2 ANSWER 10 OF 12 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2001433635 MEDLINE
DOCUMENT NUMBER: 21374019 PubMed ID: 11481274
TITLE: Proliferation, migration, and ERK activation in human ***retinal*** endothelial cells through A(2B) adenosine receptor stimulation.
AUTHOR: Grant M B; Davis M I; Caballero S; Feoktistov I; Biaggioni I; Belardinelli L
CORPORATE SOURCE: Department of Medicine, University of Florida, Gainesville 32610-0267, USA.. grantma@pharmacology.ufl.edu
SOURCE: INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE, (2001 Aug) 42 (9) 2068-73.
Journal code: 7703701. ISSN: 0146-0404.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010820
Last Updated on STN: 20010820
Entered Medline: 20010816

TI Proliferation, migration, and ERK activation in human ***retinal*** endothelial cells through A(2B) adenosine receptor stimulation.

AB . . . study demonstrated that activation of the A(2B) adenosine receptor (AdoR) increases cAMP accumulation, cell proliferation, and VEGF expression in human ***retinal*** endothelial cells (HRECs). In the present study, the role of this receptor was further characterized by examination of the effects of the selective A(2B) AdoR antagonists 3-N-propylxanthine (***enprofylline***) and 3-isobutyl-8-pyrrolidinoxanthine (IPDX) on AdoR-mediated HREC proliferation, capillary tube formation, and signal-transduction pathways. METHODS: HRECs were exposed to the adenosine. . . cells grown on a synthetic basement membrane matrix. RESULTS: NECA induced proliferation in a concentration-dependent manner that was inhibited by ***enprofylline*** and IPDX. NECA stimulated chemotaxis in a concentration-dependent manner that was also blocked by both A(2B) AdoR antagonists. NECA activated. . . enhanced tube formation on the matrix, whereas both A(2B) AdoR

antagonists, ***enprofylline*** and IPDX, inhibited NECA-stimulated proliferation, ERK activation, cell migration, and capillary tube formation. A(2B) AdoR inhibition may offer a way to inhibit ***retinal*** angiogenesis and provide a novel therapeutic approach to treatment of diseases associated with aberrant neovascularization, such as diabetic retinopathy and. . .

CT . . .

antagonists & inhibitors

*Mitogen-Activated Protein Kinases: ME, metabolism

Receptors, Purinergic P1: AI, antagonists & inhibitors

*Receptors, Purinergic P1: ME, metabolism

****Retinal Vessels: ME, metabolism***

Signal Transduction

Vasodilator Agents: PD, pharmacology

L2 ANSWER 11 OF 12 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2001:321152 BIOSIS

DOCUMENT NUMBER: PREV200100321152

TITLE: A2B adenosine receptor mediates proliferation, migration, and activation of ERK in human ***retinal*** endothelial cells.

AUTHOR(S): Caballero, S. [Reprint author]; Davis, M. I. [Reprint author]; Grant, M. B. [Reprint author]

CORPORATE SOURCE: Pharmacology and Therapeutics, University of Florida, Gainesville, FL, USA

SOURCE: IOVS, (March 15, 2001) Vol. 42, No. 4, pp. S244. print. Meeting Info.: Annual Meeting of the Association for Research in Vision and Ophthalmology. Fort Lauderdale, Florida, USA. April 29-May 04, 2001.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 4 Jul 2001
Last Updated on STN: 19 Feb 2002

TI A2B adenosine receptor mediates proliferation, migration, and activation of ERK in human ***retinal*** endothelial cells.

IT . . .
Sense Organs (Sensory Reception); Cardiovascular System (Transport and Circulation)

IT Parts, Structures, & Systems of Organisms
capillary tube: circulatory system; ***retina*** : sensory system; ***retinal*** endothelial cell: sensory system

IT Chemicals & Biochemicals
5'-N-ethylcarboxamido-adenosine [NECA]; A-2B adenosine receptor; H-89; JW-VI-08: adenosine receptor antagonist; PD98059: enzyme inhibitor; cAMP [cyclic AMP]; cyclic AMP-response element binding protein [CREB]; ***enprofylline*** : adenosine receptor antagonist; extracellular signal-regulated kinase [ERK]: activation, migration, proliferation; mitogen activated protein kinase kinase [MEK]

IT Miscellaneous Descriptors
capillary tube formation; chemotaxis; ***retinal*** angiogenesis; Meeting Abstract

RN 35920-39-9 (5'-N-ethylcarboxamido-adenosine)
35920-39-9 (NECA)
167869-21-8 (PD98059)
60-92-4 (cAMP)
60-92-4 (cyclic AMP)
41078-02-8 (***enprofylline***)
142243-02-5 (extracellular signal-regulated kinase)
142243-02-5 (ERK)
142805-58-1 (mitogen activated protein kinase kinase)
142805-58-1 (MEK)

L2 ANSWER 12 OF 12 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2001:451406 BIOSIS

DOCUMENT NUMBER: PREV200100451406

TITLE: Proliferation, migration, and signal transduction in human ***retinal*** endothelial cells mediated by the A2B adenosine receptor.

AUTHOR(S): Grant, Maria B. [Reprint author]; Davis, Margaret I. [Reprint author]; Caballero, Sergio [Reprint author]

CORPORATE SOURCE: Gainesville, FL, USA

SOURCE: Diabetes, (June, 2001) Vol. 50, No. Supplement 2, pp. A18. print.
Meeting Info.: 61st Scientific Sessions of the American Diabetes Association. Philadelphia, Pennsylvania, USA. June

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                    CODEN: DIAEAZ. ISSN: 0012-1797.
DOCUMENT TYPE:      Conference; (Meeting)
                    Conference; Abstract; (Meeting Abstract)
LANGUAGE:           English
ENTRY DATE:         Entered STN: 19 Sep 2001
                    Last Updated on STN: 22 Feb 2002
TI   Proliferation, migration, and signal transduction in human   ***retinal***
     endothelial cells mediated by the A2B adenosine receptor.
IT   . . .
        Organs (Sensory Reception); Cardiovascular System (Transport and
        Circulation)
IT   Parts, Structures, & Systems of Organisms
        capillary tube: circulatory system, formation;   ***retina***  :
        sensory system
IT   Chemicals & Biochemicals
        5'-N-ethylcarboxamido-adenosine [NECA]: adenosine analogue; A2B:
        adenosine receptor; H-89: protein inhibitor; JW-VI-08: adenosine
        receptor antagonist;. . . [mitogen-activated protein kinase]:
        regulation; PD98059: enzyme inhibitor; adenosine; cAMP response element
        binding protein [cyclic AMP response element binding protein]:
        regulation;   ***enprofylline***  : adenosine receptor antagonist;
        extracellular signal-regulated kinase [ERK]: regulation
IT   Miscellaneous Descriptors
        chemotaxis;   ***retinal***   angiogenesis; signal transduction
        pathway; Meeting Abstract
ORGN Classifier
        Hominidae   86215
     Super Taxa
        Primates; Mammalia; Vertebrata; Chordata; Animalia
     Organism Name
        HREC cell line: human   ***retinal***   endothelial cells, migration,
        proliferation, signal transduction
     Taxa Notes
        Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN   35920-39-9 (5'-N-ethylcarboxamido-adenosine)
     35920-39-9 (NECA)
     142243-02-5 (MAP kinase)
     142243-02-5 (mitogen-activated protein kinase)
     167869-21-8 (PD98059)
     58-61-7 (adenosine)
     41078-02-8 (  ***enprofylline***  )
     142243-02-5 (extracellular signal-regulated kinase)
     142243-02-5 (ERK)


=> s 3()n()propylxanthine
L3          44 3(W) N(W) PROPYLXANTHINE

=> s l3 and (retina or retinal)
L4           5 L3 AND (RETINA OR RETINAL)

=> d history

     (FILE 'HOME' ENTERED AT 12:54:00 ON 21 JAN 2004)

     FILE 'MEDLINE, CAPLUS, LIFESCI, EMBASE, USPATFULL, BIOSIS' ENTERED AT
     12:54:17 ON 21 JAN 2004
L1           14 S ENPROFYLLINE AND (RETINA OR RETINAL)
L2           12 DUP REM L1 (2 DUPLICATES REMOVED)
L3           44 S 3()N()PROPYLXANTHINE
L4            5 S L3 AND (RETINA OR RETINAL)

=> s l4 not l1
L5           1 L4 NOT L1

=> d l5 ibib abs tot

L5   ANSWER 1 OF 1  USPATFULL on STN
ACCESSION NUMBER:       2002:4163  USPATFULL
TITLE:                  Method for identifying and using A2B adenosine receptor
                        antagonists to mediate mammalian cell proliferation
INVENTOR(S):            Belardinelli, Luiz, Menlo Park, CA, UNITED STATES
                        Grant, Maria B., Archer, FL, UNITED STATES

                             NUMBER       KIND    DATE
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APPLICATION INFO.:      US 2001-785895     A1   20010216  (9)

                              NUMBER         DATE
                        ------------------ --------
PRIORITY INFORMATION:   US 2000-183141P    20000217 (60)
DOCUMENT TYPE:          Utility
FILE SEGMENT:           APPLICATION
LEGAL REPRESENTATIVE:   A. Blair Hughes, McDonnell Boehnen Hulbert & Berghoff,
                        32nd Floor, 300 S. Wacker Drive, Chicago, IL, 60606
NUMBER OF CLAIMS:       18
EXEMPLARY CLAIM:        1
NUMBER OF DRAWINGS:     3 Drawing Page(s)
LINE COUNT:             453
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB      This invention concerns methods for identifying A.sub.2B adenosine
        receptor agonists and antagonists as well as methods for using A.sub.2B.
        adenosine receptor antagonists to treat cell proliferation orders
        mediated by the A.sub.2B adenosine receptor.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.


=> d history

     (FILE 'HOME' ENTERED AT 12:54:00 ON 21 JAN 2004)

     FILE 'MEDLINE, CAPLUS, LIFESCI, EMBASE, USPATFULL, BIOSIS' ENTERED AT
     12:54:17 ON 21 JAN 2004
L1            14 S ENPROFYLLINE AND (RETINA OR RETINAL)
L2            12 DUP REM L1 (2 DUPLICATES REMOVED)
L3            44 S 3()N()PROPYLXANTHINE
L4             5 S L3 AND (RETINA OR RETINAL)
L5             1 S L4 NOT L1

=> dup rem l3
PROCESSING COMPLETED FOR L3
L6            28 DUP REM L3 (16 DUPLICATES REMOVED)

=> d l6 ibib abs tot

L6   ANSWER 1 OF 28  USPATFULL on STN
ACCESSION NUMBER:       2004:7842  USPATFULL
TITLE:                  2-Aminopyridine compounds and use thereof as drugs
INVENTOR(S):            Harada, Hitoshi, Ibaraki, JAPAN
                        Asano, Osamu, Ibaraki, JAPAN
                        Miyazawa, Shuhei, Ibaraki, JAPAN
                        Ueda, Masato, Ibaraki, JAPAN
                        Yasuda, Masahiro, Ibaraki, JAPAN
                        Yasuda, Nobuyuki, Ibaraki, JAPAN

                             NUMBER        KIND    DATE
                        ---------------- ------ --------
PATENT INFORMATION:     US 2004006082      A1   20040108
APPLICATION INFO.:      US 2003-333689     A1   20030123  (10)
                        WO 2001-JP6870          20010809

                              NUMBER         DATE
                        ------------------ --------
PRIORITY INFORMATION:   JP 2000-245056     20000811
DOCUMENT TYPE:          Utility
FILE SEGMENT:           APPLICATION
LEGAL REPRESENTATIVE:   BIRCH STEWART KOLASCH & BIRCH, PO BOX 747, FALLS
                        CHURCH, VA, 22040-0747
NUMBER OF CLAIMS:       40
EXEMPLARY CLAIM:        1
LINE COUNT:             3562
AB      The present invention provides 2-aminopyridine compound having an
        excellent adenosine receptor (A.sub.1, A.sub.2a, A.sub.2b receptors)
        antagonism, which is represented by the following formula:   ##STR1##

        (wherein, R.sup.1 represents cyano group, carboxyl group or an
        optionally substituted carbamoyl group; R.sup.2 represents hydrogen
        atom, hydroxyl group, an optionally substituted C.sub.1-6 alkoxy group,
        an optionally substituted C.sub.6-14 aromatic hydrocarbon cyclic group
        or an optionally substituted 5- to 14-membered aromatic heterocyclic
        group; and R.sup.3 and R.sup.4 are the same as or different from each
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group, a 5- to 14-membered non-aromatic heterocyclic group or a 5- to 14-membered aromatic heterocyclic group which may be substituted, respectively) or a salt thereof.

L6 ANSWER 2 OF 28 USPATFULL on STN
ACCESSION NUMBER: 2003:244969 USPATFULL
TITLE: Medicinal compositions promoting bowel movement
INVENTOR(S): Yasuda, Masahiro, Ibaraki, JAPAN
Harada, Hitoshi, Ibaraki, JAPAN
Miyazawa, Shuhei, Ibaraki, JAPAN
Kobayashi, Seiichi, Belmont, MA, UNITED STATES
Harada, Kokichi, Ibaraki, JAPAN
Hida, Takayuki, Ibaraki, JAPAN
Shibata, Hisashi, Ibaraki, JAPAN
Yasuda, Nobuyuki, Ibaraki, JAPAN
Asano, Osamu, Ibaraki, JAPAN
Kotake, Yoshihiko, Ibaraki, JAPAN

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003171383	A1	20030911	
APPLICATION INFO.:	US 2002-257091	A1	20021009	(10)
	WO 2001-JP3643		20010426	

	NUMBER	DATE
PRIORITY INFORMATION:	JP 2000-126489	20000426
	JP 2000-220124	20000721

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BIRCH STEWART KOLASCH & BIRCH, PO BOX 747, FALLS CHURCH, VA, 22040-0747
NUMBER OF CLAIMS: 31
EXEMPLARY CLAIM: 1
LINE COUNT: 2491
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a medicament having a gentle but strong defecation-promoting action without causing diarrhea. That is, it provides a defecation-promoting agent comprising a compound having an adenosine A.sub.2 receptor antagonism, preferably an adenosine A.sub.2b receptor antagonism, or a salt thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 3 OF 28 USPATFULL on STN
ACCESSION NUMBER: 2003:195050 USPATFULL
TITLE: Transmucosal phosphodiesterase inhibitors for the treatment of erectile dysfunction
INVENTOR(S): Doherty, Paul C., JR., Cupertino, CA, UNITED STATES
Place, Virgil A., Kawaihae, HI, UNITED STATES
Smith, William L., Mahwah, NJ, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003134861	A1	20030717	
APPLICATION INFO.:	US 2003-351198	A1	20030124	(10)

RELATED APPLN. INFO.: Division of Ser. No. US 1999-467094, filed on 10 Dec 1999, GRANTED, Pat. No. US 6548490 Continuation-in-part of Ser. No. US 1998-181070, filed on 27 Oct 1998, GRANTED, Pat. No. US 6037346 Continuation-in-part of Ser. No. US 1997-958816, filed on 28 Oct 1997, ABANDONED
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: REED & EBERLE LLP, 800 MENLO AVENUE, SUITE 210, MENLO PARK, CA, 94025
NUMBER OF CLAIMS: 42
EXEMPLARY CLAIM: 1
LINE COUNT: 1138
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A pharmaceutical formulation is provided for treating erectile dysfunction in a mammalian male individual. The pharmaceutical formulation includes a phosphodiesterase inhibitor or a pharmaceutically acceptable salt, ester, amide or derivative thereof, that is administered transmucosally within the context of an effective dosing

sublingual and transrectal routes. A kit for the administration of the pharmaceutical formulation is also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 4 OF 28 USPATFULL on STN

ACCESSION NUMBER:	2003:102369 USPATFULL
TITLE:	Transmucosal administration of phosphodiesterase inhibitors for the treatment of erectile dysfunction
INVENTOR(S):	Doherty, Jr., Paul C., Cupertino, CA, United States Place, Virgil A., Kawaihae, HI, United States Smith, William L., Mahwah, NJ, United States
PATENT ASSIGNEE(S):	Vivus, Inc., Mountain View, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6548490	B1	20030415
APPLICATION INFO.:	US 1999-467094		19991210 (9)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1998-181070, filed on 27 Oct 1998, now patented, Pat. No. US 6037346 Continuation-in-part of Ser. No. US 1997-958816, filed on 28 Oct 1997, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	GRANTED		
PRIMARY EXAMINER:	Reamer, James H.		
LEGAL REPRESENTATIVE:	Reed, Dianne E., Reed & Associates		
NUMBER OF CLAIMS:	51		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	0 Drawing Figure(s); 0 Drawing Page(s)		
LINE COUNT:	1240		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method is provided for treating erectile dysfunction in a mammalian male individual. The method involves the transmucosal administration of a phosphodiesterase inhibitor or a pharmaceutically acceptable salt, ester, amide or derivative thereof, within the context of an effective dosing regimen. Preferred modes of administration include transbuccal, sublingual and transrectal routes. Pharmaceutical formulations and kits are provided as well.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 5 OF 28 USPATFULL on STN

ACCESSION NUMBER:	2002:295156 USPATFULL
TITLE:	Compounds for inhibition of ceramide-mediated signal transduction
INVENTOR(S):	Carson, Dennis A., Del Mar, CA, UNITED STATES Cottam, Howard, Fallbrook, CA, UNITED STATES
PATENT ASSIGNEE(S):	The Regents of the University of California (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002165202	A1	20021107
	US 6562819	B2	20030513
APPLICATION INFO.:	US 2001-951198	A1	20010913 (9)
RELATED APPLN. INFO.:	Division of Ser. No. US 1997-858778, filed on 19 May 1997, PATENTED Continuation-in-part of Ser. No. US 1994-367102, filed on 29 Dec 1994, ABANDONED Continuation-in-part of Ser. No. US 1995-482551, filed on 7 Jun 1995, PATENTED		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A., P.O. BOX 2938, MINNEAPOLIS, MN, 55402		
NUMBER OF CLAIMS:	22		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	14 Drawing Page(s)		
LINE COUNT:	1619		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel, heterocyclic compounds having at least one ring nitrogen, disclosed side chains and, in some embodiments, an oxygen ortho to the ring nitrogen inhibit inflammatory responses associated with TNF-.alpha. and fibroblast proliferation in vivo and in vitro. The compounds of the invention neither appreciably inhibit the activity of cAMP phosphodiesterase nor the hydrolysis of phosphatidic acid, and are

are esters. Methods for the use of the novel compounds to inhibit ceramide-mediated intracellular responses in stimuli in vivo (particularly TN-.alpha.) are also described. The methods are expected to be of use in reducing inflammatory responses (for example, after angioplasty), in limiting fibrosis (for example, of the liver in cirrhosis), in inhibiting cell senescence, cell apoptosis and UV induced cutaneous immune suppression. Compounds having enhanced water solubility are also described.

AS INDEXING IS AVAILABLE FOR THIS PATENT.

6 ANSWER 6 OF 28 USPATFULL on STN
CCESSION NUMBER: 2002:67175 USPATFULL
ITLE: Administration of phosphodiesterase inhibitors for the treatment of premature ejaculation
NVENTOR(S): Wilson, Leland F., Menlo Park, CA, UNITED STATES
Doherty, Paul C., JR., Cupertino, CA, UNITED STATES
Place, Virgil A., Kawaihae, HI, UNITED STATES
Smith, William L., Montclair, NJ, UNITED STATES
Abdel-Hamid Abdou Ali, Ibrahim AbouBakr, Mansoura, EGYPT

	NUMBER	KIND	DATE
ATENT INFORMATION:	US 2002037828	A1	20020328
	US 6403597	B2	20020611
PPLICATION INFO.:	US 2001-888250	A1	20010621 (9)

ELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1999-467094, filed on 10 Dec 1999, PENDING Continuation-in-part of Ser. No. US 1998-181070, filed on 27 Oct 1998, GRANTED, Pat. No. US 6037346 Continuation-in-part of Ser. No. US 1997-958816, filed on 28 Oct 1997, ABANDONED
OCUMENT TYPE: Utility
ILE SEGMENT: APPLICATION
EGAL REPRESENTATIVE: REED & ASSOCIATES, 800 MENLO AVENUE, SUITE 210, MENLO PARK, CA, 94025
UMBER OF CLAIMS: 94
XEMPLARY CLAIM: 1
UMBER OF DRAWINGS: 1 Drawing Page(s)
INE COUNT: 2011
AS INDEXING IS AVAILABLE FOR THIS PATENT.
B A method is provided for treatment of premature ejaculation by administration of a phosphodiesterase inhibitor, e.g., an inhibitor of a Type III, Type IV, or Type V phosphodiesterase. In a preferred embodiment, administration is on as "as needed" basis, i.e., the drug is administered immediately or several hours prior to sexual activity. Pharmaceutical formulations and packaged kits are also provided.

AS INDEXING IS AVAILABLE FOR THIS PATENT.

6 ANSWER 7 OF 28 USPATFULL on STN
CCESSION NUMBER: 2002:8498 USPATFULL
ITLE: Transmucosal administration of phosphodiesterase inhibitors for the treatment of erectile dysfunction
NVENTOR(S): Doherty, Paul C., JR., Cupertino, CA, UNITED STATES
Place, Virgil A., Kawaihae, HI, UNITED STATES
Smith, William L., Mahwah, NJ, UNITED STATES

	NUMBER	KIND	DATE
ATENT INFORMATION:	US 2002004498	A1	20020110
PPLICATION INFO.:	US 2001-938417	A1	20010823 (9)

ELATED APPLN. INFO.: Continuation of Ser. No. US 1999-467094, filed on 10 Dec 1999, PENDING Continuation-in-part of Ser. No. US 1998-181070, filed on 27 Oct 1998, GRANTED, Pat. No. US 6037346 Continuation-in-part of Ser. No. US 1997-958816, filed on 28 Oct 1997, ABANDONED
OCUMENT TYPE: Utility
ILE SEGMENT: APPLICATION
EGAL REPRESENTATIVE: REED & ASSOCIATES, 800 MENLO AVENUE, SUITE 210, MENLO PARK, CA, 94025
UMBER OF CLAIMS: 58
XEMPLARY CLAIM: 1
INE COUNT: 1200
AS INDEXING IS AVAILABLE FOR THIS PATENT.
B A method is provided for treating erectile dysfunction in a mammalian

a phosphodiesterase inhibitor or a pharmaceutically acceptable salt, ester, amide or derivative thereof, within the context of an effective dosing regimen. Preferred modes of administration include transbuccal, sublingual and transrectal routes. Pharmaceutical formulations and kits are provided as well.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 8 OF 28 USPATFULL on STN
ACCESSION NUMBER: 2002:4163 USPATFULL
TITLE: Method for identifying and using A2B adenosine receptor antagonists to mediate mammalian cell proliferation
INVENTOR(S): Belardinelli, Luiz, Menlo Park, CA, UNITED STATES
Grant, Maria B., Archer, FL, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002002142	A1	20020103
APPLICATION INFO.:	US 2001-785895	A1	20010216 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-183141P	20000217 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: A. Blair Hughes, McDonnell Boehnen Hulbert & Berghoff, 32nd Floor, 300 S. Wacker Drive, Chicago, IL, 60606
NUMBER OF CLAIMS: 18
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Page(s)
LINE COUNT: 453
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention concerns methods for identifying A.sub.2B adenosine receptor agonists and antagonists as well as methods for using A.sub.2B. adenosine receptor antagonists to treat cell proliferation orders mediated by the A.sub.2B adenosine receptor.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 9 OF 28 USPATFULL on STN
ACCESSION NUMBER: 2001:215051 USPATFULL
TITLE: Compounds for inhibition of ceramide-mediated signal transduction
INVENTOR(S): Carson, Dennis A., Del Mar, CA, United States
Cottam, Howard, Fallbrook, CA, United States
PATENT ASSIGNEE(S): The Regents of the University of California, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6323201	B1	20011127
APPLICATION INFO.:	US 1997-858778		19970519 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1995-482551, filed on 7 Jun 1995, now patented, Pat. No. US 5843943
Continuation-in-part of Ser. No. US 1994-367102, filed on 29 Dec 1994, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Ford, John M.
LEGAL REPRESENTATIVE: Schwegman, Lundberg, Woessner & Kluth, P.A.
NUMBER OF CLAIMS: 18
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 23 Drawing Figure(s); 14 Drawing Page(s)
LINE COUNT: 1528
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel, heterocyclic compounds having at least one ring nitrogen, disclosed side chains and, in some embodiments, an oxygen ortho to the ring nitrogen inhibit inflammatory responses associated with TNF-.alpha. and fibroblast proliferation in vivo and in vitro. The compounds of the invention neither appreciably inhibit the activity of cAMP phosphodiesterase nor the hydrolysis of phosphatidic acid, and are neither cytotoxic nor cytostatic. Preferred compounds of the invention are esters. Methods for the use of the novel compounds to inhibit ceramide-mediated intracellular responses in stimuli in vivo (particularly TN-.alpha.) are also described. The methods are expected to be of use in reducing inflammatory responses (for example, after

cirrhosis), in inhibiting cell senescence, cell apoptosis and UV induced cutaneous immune suppression. Compounds having enhanced water solubility are also described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 10 OF 28 USPATFULL on STN

ACCESSION NUMBER:	2001:52215 USPATFULL
TITLE:	Use of theophylline derivatives for the treatment and prophylaxis of states of shock, novel xanthine compounds and processes for their preparation
INVENTOR(S):	Gebert, Ulrich, Glashutten, Germany, Federal Republic of Wolf, Erhard, Hofheim, Germany, Federal Republic of Defossa, Elisabeth, Idstein, Germany, Federal Republic of Heinelt, Uwe, Wiesbaden, Germany, Federal Republic of Anagnostopulos, Hiristo, Wiesbaden, Germany, Federal Republic of Rudolphi, Karl, Mainz, Germany, Federal Republic of Grome, John J., Wiesbaden, Germany, Federal Republic of
PATENT ASSIGNEE(S):	Hoechst Aktiengesellschaft, Frankfurt am Main, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6214992	B1	20010410	
APPLICATION INFO.:	US 1997-868641		19970604	(8)

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1996-19622737	19960607
	DE 1996-19629815	19960724

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Berch, Mark L.
LEGAL REPRESENTATIVE:	Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.
NUMBER OF CLAIMS:	24
EXEMPLARY CLAIM:	1
LINE COUNT:	1716

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Theophylline derivatives having at least one ether function in the structurally modified methyl radical in the 1-position that are useful in the treatment and prophylaxis of states of shock, new xanthine compounds having this substitution pattern, and processes for their preparation.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 11 OF 28 MEDLINE on STN

ACCESSION NUMBER:	2001700409 MEDLINE
DOCUMENT NUMBER:	21583628 PubMed ID: 11726639
TITLE:	Adenosine receptor antagonists and retinal neovascularization in vivo.
AUTHOR:	Mino R P; Spoerri P E; Caballero S; Player D; Belardinelli L; Biaggioni I; Grant M B
CORPORATE SOURCE:	Department of Molecular Biology and Genetics, University of Florida, Gainesville, FL 32610-0267, USA.
SOURCE:	INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE, (2001 Dec) 42 (13) 3320-4. Journal code: 7703701. ISSN: 0146-0404.
PUB. COUNTRY:	United States
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals; Space Life Sciences
ENTRY MONTH:	200201
ENTRY DATE:	Entered STN: 20011220 Last Updated on STN: 20020216 Entered Medline: 20020115

AB PURPOSE: The role of adenosine receptor (AdoR) antagonists in human retinal endothelial cell function in vitro has previously been determined. In this study, efficacy of AdoR antagonist administration in reducing retinal neovascularization was examined in a mouse pup model of oxygen-induced retinopathy. METHODS: A previously described model of oxygen-induced retinal neovascularization in newborn mouse pups was used to examine the effect of various AdoR antagonists on neovascularization.

A(2A)-selective antagonist ZM241385, the A(2B)-selective antagonists ***3*** - ***N*** - ***propylxanthine*** (enprofylline) and 3-isobutyl-8-pyrrolidinoxanthine (IPDX), and the A(1)-selective antagonist cyclopentyl-1,3-dipropylxanthine (CPX) were used. After the hyperoxia exposure the animals received daily intraperitoneal injections of pharmacologically relevant doses of AdoR antagonists for 5 days. Control animals received vehicle (0.1% dimethyl sulfoxide [DMSO]) alone. The animals were then killed and perfused with fluorescein-dextran. Wholemounts of retinas from one eye were prepared and examined, whereas the retinas of the contralateral eye were embedded, sectioned, and stained for counting neovascular nuclei extending beyond the internal limiting membrane into the vitreous. RESULTS: Angiography of wholemount retinas showed reduction of neovascular tufts in animals treated with selective A(2B) AdoR antagonists. Quantification of the extraretinal neovascular nuclei showed that only animals treated with XAC, enprofylline, or IPDX showed a significant reduction in retinal neovascularization. By contrast, neither CPX nor ZM241385 had an effect on neovascularization. CONCLUSIONS: The A(2B)-selective AdoR antagonists inhibited oxygen-induced retinal neovascularization in vivo and may provide a basis for developing pharmacologic therapies for the treatment of proliferative retinopathies.

L6 ANSWER 12 OF 28 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2001433635 MEDLINE
DOCUMENT NUMBER: 21374019 PubMed ID: 11481274
TITLE: Proliferation, migration, and ERK activation in human retinal endothelial cells through A(2B) adenosine receptor stimulation.
AUTHOR: Grant M B; Davis M I; Caballero S; Feoktistov I; Biaggioni I; Belardinelli L
CORPORATE SOURCE: Department of Medicine, University of Florida, Gainesville 32610-0267, USA.. grantma@pharmacology.ufl.edu
SOURCE: INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE, (2001 Aug) 42 (9) 2068-73.
Journal code: 7703701. ISSN: 0146-0404.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010820
Last Updated on STN: 20010820
Entered Medline: 20010816

AB PURPOSE: The nucleoside adenosine has been implicated in angiogenesis. A previous study demonstrated that activation of the A(2B) adenosine receptor (AdoR) increases cAMP accumulation, cell proliferation, and VEGF expression in human retinal endothelial cells (HRECs). In the present study, the role of this receptor was further characterized by examination of the effects of the selective A(2B) AdoR antagonists ***3*** - ***N*** - ***propylxanthine*** (enprofylline) and 3-isobutyl-8-pyrrolidinoxanthine (IPDX) on AdoR-mediated HREC proliferation, capillary tube formation, and signal-transduction pathways. METHODS: HRECs were exposed to the adenosine analogue 5'-N-ethylcarboxamido-adenosine (NECA) in the absence or presence of AdoR antagonists. Migration was measured using Boyden chambers. Proliferation was assessed by counting cells. Western analysis was used to assess extracellular signal-related kinase (ERK) and cAMP response element-binding protein (CREB) in cell lysates. The effect of AdoR activation on tube formation was studied using cells grown on a synthetic basement membrane matrix. RESULTS: NECA induced proliferation in a concentration-dependent manner that was inhibited by enprofylline and IPDX. NECA stimulated chemotaxis in a concentration-dependent manner that was also blocked by both A(2B) AdoR antagonists. NECA activated ERK and CREB in HRECs. Both A(2B) AdoR antagonists diminished activation of ERK by NECA exposure. ERK activation was also blocked by the ERK-mitogen-activated protein kinase (MAPK) inhibitor PD98059, but not by the protein kinase A (PKA) inhibitor H-89. CREB activation was blocked by H-89, but not by PD98059, suggesting that ERK activation is independent of PKA. NECA enhanced tube formation on the matrix, whereas both A(2B) AdoR antagonists attenuated this effect. CONCLUSIONS: The selective A(2B) AdoR antagonists, enprofylline and IPDX, inhibited NECA-stimulated proliferation, ERK activation, cell migration, and capillary tube formation. A(2B) AdoR inhibition may offer a way to inhibit retinal angiogenesis and provide a novel therapeutic approach to treatment of diseases associated with aberrant neovascularization, such as diabetic retinopathy and retinopathy of prematurity.

L6 ANSWER 13 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2

DOCUMENT NUMBER: 132:318044
TITLE: Method for improving insulin sensitivity using an adenosine receptor antagonist
INVENTOR(S): Lanoue, Kathryn F.; Crist, George H.; Linden, Joel M.
PATENT ASSIGNEE(S): The Penn State Research Foundation, USA
SOURCE: U.S., 22 pp., Cont.-in-part of U.S. Ser. No. 86,101, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6060481	A	20000509	US 1999-259201	19990301

PRIORITY APPLN. INFO.: US 1998-86101 19980528
AB The invention relates to methods for improving insulin sensitivity in a patient using one or more A2B adenosine receptor antagonists [e.g. ***3*** - ***n*** - ***propylxanthine***] are disclosed. These methods stimulate insulin dependent glucose uptake in muscle.
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 14 OF 28 USPATFULL on STN
ACCESSION NUMBER: 2000:164509 USPATFULL
TITLE: Local administration of type III phosphodiesterase inhibitors for the treatment of erectile dysfunction
INVENTOR(S): Doherty, Jr., Paul C., Cupertino, CA, United States
Place, Virgil A., Kawaihae, HI, United States
Smith, William L., Mahwah, NJ, United States
PATENT ASSIGNEE(S): Vivus, Inc., Mountain View, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6156753		20001205
APPLICATION INFO.:	US 1999-437682		19991110 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1998-181070, filed on 27 Oct 1998, now patented, Pat. No. US 6037346 which is a continuation-in-part of Ser. No. US 1997-958816, filed on 28 Oct 1997, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Reamer, James H.
LEGAL REPRESENTATIVE: Reed, Dianne E.Reed & Associates
NUMBER OF CLAIMS: 67
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Figure(s); 4 Drawing Page(s)
LINE COUNT: 1246
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method is provided for treating erectile dysfunction, e.g., vasculogenic erectile dysfunction such as vasculogenic impotence. The method involves the administration of a Type III phosphodiesterase inhibitor or a pharmaceutically acceptable salt, ester, amide or derivative thereof, wherein administration is transurethral, topical or transdermal. A preferred mode of administration is transurethral. Pharmaceutical formulations and kits are provided as well.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 15 OF 28 USPATFULL on STN
ACCESSION NUMBER: 2000:131835 USPATFULL
TITLE: Local administration of Type IV phosphodiesterase inhibitors for the treatment of erectile dysfunction
INVENTOR(S): Doherty, Jr., Paul C., Cupertino, CA, United States
Place, Virgil A., Kawaihae, HI, United States
Smith, William L., Montclair, NJ, United States
PATENT ASSIGNEE(S): Vivus, Inc., Mountain View, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6127363		20001003
APPLICATION INFO.:	US 1999-437999		19991110 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1998-181070, filed

is a continuation-in-part of Ser. No. US 1997-958816, filed on 28 Oct 1997, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Reamer, James H.
LEGAL REPRESENTATIVE: Reed, Dianne E.Reed & Associates
NUMBER OF CLAIMS: 106
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Figure(s); 4 Drawing Page(s)
LINE COUNT: 1455
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method is provided for treating erectile dysfunction, e.g., vasculogenic erectile dysfunction such as vasculogenic impotence. The method involves the administration of a Type IV phosphodiesterase inhibitor or a pharmaceutically acceptable salt, ester, amide or derivative thereof, wherein administration is local, i.e., transurethral, intracavernosal, topical or transdermal. A preferred mode of administration is transurethral. Pharmaceutical formulations and kits are provided as well.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 16 OF 28 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 1999288734 MEDLINE
DOCUMENT NUMBER: 99288734 PubMed ID: 10361888
TITLE: Effects of XT-44, a phosphodiesterase 4 inhibitor, in osteoblastgenesis and osteoclastgenesis in culture and its therapeutic effects in rat osteopenia models.
AUTHOR: Waki Y; Horita T; Miyamoto K; Ohya K; Kasugai S
CORPORATE SOURCE: Department of Pharmacology, Faculty of Dentistry, Tokyo Medical and Dental University, Japan.
SOURCE: JAPANESE JOURNAL OF PHARMACOLOGY, (1999 Apr) 79 (4) 477-83. Journal code: 2983305R. ISSN: 0021-5198.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990727
Last Updated on STN: 20000303
Entered Medline: 19990712
AB We have reported that denbufylline, a phosphodiesterase 4 (PDE4) inhibitor, inhibits bone loss in Walker256/S tumor-bearing rats, suggesting therapeutic potentiality of a PDE4 inhibitor in osteopenia. In the present study, effects of a new PDE4 inhibitor, 1-n-butyl- ***3*** - ***n*** - ***propylxanthine*** (XT-44), in bone were evaluated in cell cultures and animal experiments. In rat bone marrow culture, XT-44 stimulated mineralized-nodule formation, whereas it inhibited osteoclast-like cell formation in mouse bone marrow culture. In Walker256/S-bearing rats (6-week-old female Wistar Imamichi rats), rapid decrease in bone mineral density (BMD) was prominent, and oral administration of XT-44 (0.3 mg/kg, every 2 days) inhibited the decrease in BMD. In the second animal experiment, female Wistar rats (6-week-old) were sciatic neurectomized, and XT-44 was orally administered to these rats every 2 days for 4 weeks. XT-44 administration (0.3 mg/kg) recovered BMD in these neurectomized animals. Furthermore, 19-week-old, female Wistar rats were ovariectomized (OVX), and 15 weeks after surgery, these rats were orally administered XT-44 every 2 days for 8 weeks. XT-44 treatment (1 mg/kg) increased the BMD of OVX rats. These results indicate that XT-44 could be a candidate as a therapeutic drug for treating osteopenia including osteoporosis.

L6 ANSWER 17 OF 28 USPATFULL on STN
ACCESSION NUMBER: 1998:150945 USPATFULL
TITLE: Compounds for inhibition of ceramide-mediated signal transduction
INVENTOR(S): Carson, Dennis A., Del Mar, CA, United States
Cottam, Howard B., Fallbrook, CA, United States
Wasson, D. Bruce, San Diego, CA, United States
PATENT ASSIGNEE(S): The Regents of the University of California, Alameda, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5843943		19981201	
APPLICATION INFO.:	US 1995-482551		19950607	(8)

on 29 Dec 1994
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Ford, John M.
LEGAL REPRESENTATIVE: Fish & Richardson P.C.
NUMBER OF CLAIMS: 9
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 23 Drawing Figure(s); 14 Drawing Page(s)
LINE COUNT: 1362
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel, heterocyclic compounds having at least one ring nitrogen, disclosed side chains and, in some embodiments, an oxygen ortho to the ring nitrogen inhibit inflammatory responses associated with TNF-.alpha. and fibroblast proliferation in vivo and in vitro. The compounds of the invention neither appreciably inhibit the activity of cAMP phosphodiesterase nor the hydrolysis of phosphatidic acid, and are neither cytotoxic nor cytostatic. Preferred compounds of the invention are esters. Methods for the use of the novel compounds to inhibit ceramide-mediated intracellular responses to stimuli in vivo (particularly TNF-.alpha.) are also described. The methods are expected to be of use in reducing inflammatory responses (for example, after angioplasty), in limiting fibrosis (for example, of the liver in cirrhosis), in inhibiting cell senescence, cell apoptosis and UV induced cutaneous immune suppression.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 18 OF 28 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 96185059 MEDLINE
DOCUMENT NUMBER: 96185059 PubMed ID: 8613965
TITLE: Negative inotropic action of denbufylline through interfering with the calcium channel independently of its PDE IV inhibitory activity in guinea pig ventricle papillary muscles.
AUTHOR: Sanae F; Ohmae S; Kobayashi D; Takag K; Miyamoto K
CORPORATE SOURCE: Applied Pharmacology, Faculty of Pharmaceutical Sciences, Hokuriku University, Kanazawa, Japan.
SOURCE: JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (1996 Apr) 277 (1) 54-60.
Journal code: 0376362. ISSN: 0022-3565.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 19960613
Last Updated on STN: 19960613
Entered Medline: 19960606
AB The inotropic actions of xanthine derivatives with long alkyl chains were investigated in guinea pig ventricular papillary muscle. A potent and nonselective phosphodiesterase (PDE) inhibitor, 3-isobutyl-1-methylxanthine, elicited a positive inotropy and inhibited the negative inotropic effects of calcium channel inhibitors, as did a selective PDE III inhibitor, amrinone, and these effects were canceled by a protein kinase inhibitor, N-[2-(p-bromocinnamylamino)ethyl]-5-isoquinolinesulfonamide (H-89). However, 1,3-di-n-butyl-7-(2'oxopropyl)xanthine (denbufylline) and 1-n-butyl- ***3*** - ***n*** - ***propylxanthine*** (XT-044), which have potent and selective PDE IV-inhibitory activities, showed negative inotropic actions that became more potent in the presence of H-89. Denbufylline abolished the late restoration phase induced by ryanodine. This xanthine derivative attenuated the effects of both the calcium channel acting agents Bay K 8644 and verapamil, without interaction with caffeine and dihydropyridine calcium channel inhibitors, and denbufylline had little direct influence on the specific binding of [(3)H]azidopine and [(3)H]desmethoxyverapamil to cardiac membranes. A nonxanthine PDE IV inhibitor, Ro 20-1724, did not affect the inotropic actions of calcium channel inhibitors. The attenuation by denbufylline or XT-044 of the negative inotropic action of verapamil was not influenced by treatment with H-89. These results suggest that in the ventricular papillary muscle, these xanthine derivatives elicit negative inotropy by acting on a verapamil-sensitive site of the calcium channel without involving their PDE-inhibitory activity.

L6 ANSWER 19 OF 28 EMBASE
on STN DUPLICATE 5

DOCUMENT NUMBER: 1995365518
TITLE: Cyclic AMP-dependent and cyclic AMP-independent inotropic actions of PDE inhibitors in guinea-pig ventricular papillary muscles.
AUTHOR: Miyamoto K.-I.; Ohmae S.; Sanae F.; Sawanishi H.; Tkagi K.
CORPORATE SOURCE: Department of Applied Pharmacology, Faculty of Pharmaceutical Sciences, Hokuriku University, Ho-3 Kanagawa-machi,Kanazawa 920-11, Japan
SOURCE: Folia Pharmacologica Japonica, (1995) 106/SUPPL. 1 (182P-186P).
ISSN: 0015-5691 CODEN: NYKZAU
COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: Japanese
SUMMARY LANGUAGE: English

AB The inotropic actions of xanthine derivatives, having long alkyl chains, were investigated in guinea pig ventricular papillary muscle. A potent and nonselective phosphodiesterase (PDE) inhibitor, 3 isobutyl-1-methylxanthine, elicited a positive inotropy and inhibited the negative inotropic effects of calcium channel inhibitors, as well as a selective PDE III inhibitor, amrinone, these effects which were canceled by a protein kinase inhibitor, N- [2-(p-bromocinnamylamino)ethyl]-5 isoquinolinesulfonamide (H-89). However, 1,3-di-n-butyl-7-(2'-oxopropyl)xanthine (denbufylline)and 1-n-butyl- ***3*** - ***n*** - ***propylxanthine*** (XT-044), which possess potent and selective PDE IV inhibitory activities, showed negative inotropic actions which became more potent in the presence of H-89. Denbufylline allowed to disappear late restoration phase induced by ryanodine. This xanthine derivative attenuated the both effects of calcium channel acting agents, Bay K 8644 and verapamil, without interaction with caffeine and dihydropyridine calcium channel inhibitors. A nonxanthine PDE IV inhibitor, Ro 20-1724, did not affect the inotropic actions of calcium channel inhibitors. The attenuation by denbufylline or XT-044 of the negative inotropic action of verapamil was not influenced by pretreatment with H-89. These results suggest that these xanthine derivatives elicit negative inotropy through acting on a verapamil sensitive site of calcium channel without involving of their PDE inhibitory activity, in the ventricular papillary muscle.

L6 ANSWER 20 OF 28 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 95032159 MEDLINE
DOCUMENT NUMBER: 95032159 PubMed ID: 7945415
TITLE: Cyclic nucleotide phosphodiesterase isoenzymes in guinea-pig tracheal muscle and bronchorelaxation by alkylxanthines.
AUTHOR: Miyamoto K; Kurita M; Sakai R; Sanae F; Wakusawa S; Takagi K
CORPORATE SOURCE: Research Laboratory for Development of Medicine, Faculty of Pharmaceutical Sciences, Hokuriku University, Kanazawa, Japan.
SOURCE: BIOCHEMICAL PHARMACOLOGY, (1994 Sep 15) 48 (6) 1219-23.
Journal code: 0101032. ISSN: 0006-2952.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199411
ENTRY DATE: Entered STN: 19941222
Last Updated on STN: 19970203
Entered Medline: 19941110

AB In this study the phosphodiesterase (PDE) isoenzymes in guinea-pig trachealis smooth muscle were separated by DEAE-Sepharose anion exchange chromatography, identified, and characterized. Furthermore the effect of theophylline and 1-n-butyl- ***3*** - ***n*** - ***propylxanthine*** (BPX) on the isolated PDE isoenzymes and on their tracheal relaxant effect were investigated and compared with the nonxanthine PDE inhibitors amrinone and Ro 20-1724. We identified five distinct isoenzymes in guinea-pig tracheal muscle; calcium/calmodulin-stimulated cyclic AMP PDE (PDE I), cyclic GMP-stimulated cyclic AMP PDE (PDE II), cyclic GMP-inhibited and amrinone-sensitive cyclic AMP PDE (PDE III), cyclic AMP-specific and Ro 20-1724-sensitive PDE (PDE IV), and cyclic GMP-specific PDE (PDE V). BPX strongly inhibited the PDE IV isoenzyme with high selectivity, while the inhibitory effect of theophylline was weak. The PDE IV inhibitors BPX and Ro 20-1724 synergistically increased the relaxant effect of the beta 2-adrenoceptor agonist salbutamol in

contrast, amrinone, a PDE III inhibitor, hardly influenced the relaxant effect of salbutamol, suggesting that the PDE IV isoenzyme is functionally associated with beta 2-adrenoceptors in guinea-pig trachea and that inhibition of this enzyme potentiates the ability of salbutamol to increase the intracellular cyclic AMP content. These results indicate that the PDE IV isoenzyme plays a significant role in alkylxanthine-mediated relaxation of guinea-pig trachea.

L6 ANSWER 21 OF 28 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1994:320005 BIOSIS
DOCUMENT NUMBER: PREV199497333005
TITLE: Selective tracheal relaxation and phosphodiesterase-IV inhibition by xanthine derivatives.
AUTHOR(S): Miyamoto, Ken-Ichi [Reprint author]; Kurita, Mariko; Ohmae, Shinji; Sakai, Ryosuke; Sanae, Fujiko; Takagi, Kenzo
CORPORATE SOURCE: Res. Lab. Development Med., Fac. Pharmaceutical Sci., Hokuriku Univ., Ho-3 Kanagawa-machi, Kanazawa 920-11, Japan
SOURCE: European Journal of Pharmacology Molecular Pharmacology Section, (1994) Vol. 15, No. 3, pp. 317-322.
CODEN: EJPPET. ISSN: 0922-4106.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Jul 1994
Last Updated on STN: 27 Jul 1994
AB The effects of substitutions in the xanthine nucleus on tracheal relaxant activity, atrium chronotropic activity, adenosine A-1 affinity, and inhibitory activities on cyclic AMP-phosphodiesterase isoenzymes in guinea pigs were studied. Substitution.with a long alkyl chain at the N1-position of xanthine nucleus increased the tracheal relaxant activity without leading to positive chronotropic action, and tong alkyl chains at the N3-position increased both activities. N7-substitutions with n-propyl and 2'-oxopropyl groups, such as in denbufylline, increased bronchoselectivity. N7 substitution decreased the adenosine A-1 affinity, but substitution at either the N1- or N3-position increased it. The bronchorelaxant activity of xanthine derivatives was closely correlated with their inhibition of phosphodiesterase-IV, but not with their adenosine A-1 affinity; the positive chronotropic effects were related to their inhibition of phosphodiesterase-III. This study confirms that the bronchorelaxation of xanthine derivatives is mediated by inhibition of the isoenzyme phosphodiesterase-IV. The results of structure-activity analysis suggest that substitutions at the N1- and N7-positions should be tried in the development of xanthine derivatives that are selective bronchodilators and phosphodiesterase-IV inhibitors.

L6 ANSWER 22 OF 28 USPATFULL on STN
ACCESSION NUMBER: 93:104960 USPATFULL
TITLE: Condensed purine derivatives
INVENTOR(S): Suzuki, Fumio, Mishima, Japan
Shimada, Junichi, Shizuoka, Japan
Kuroda, Takeshi, Shizuoka, Japan
Kubo, Kazuhiro, Shizuoka, Japan
Karasawa, Akira, Huntingdon Valley, PA, United States
Ohno, Tetsuji, Shizuoka, Japan
Ohmori, Kenji, Mishima, Japan
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Tokyo, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5270316		19931214	
APPLICATION INFO.:	US 1990-599758		19901019	(7)

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1989-273403	19891020

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Shah, Mukund J.
ASSISTANT EXAMINER: Bernhardt, E.
LEGAL REPRESENTATIVE: Fitzpatrick, Cella, Harper & Scinto
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
LINE COUNT: 1620
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB There are disclosed condensed purine derivatives represented by formula; ##STR1## in which R.sup.3 represents hydrogen, lower alkyl or benzyl;

alkyl, aralkyl or phenyl; and n is an integer of 0 or 1; R.sup.1 represents hydrogen, lower alkyl, alicyclic alkyl, noradamantan-3-yl, dicyclopropylmethyl or styryl; and R.sup.2 represents hydrogen, lower alkyl or alicyclic alkyl; or a pharmaceutically acceptable salt thereof. The derivatives and pharmaceutically acceptable salts are useful as diuretics, renal protecting agents, antiallergic agents and hypotensives.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 23 OF 28 USPATFULL on STN

ACCESSION NUMBER:	92:104979 USPATFULL
TITLE:	s-Triazolo(3,4-I)purine derivatives
INVENTOR(S):	Suzuki, Fumio, Mishima, Japan Shimada, Junichi, Shizuoka, Japan Ohmori, Kenji, Mishima, Japan Manabe, Haruhiko, Shizuoka, Japan Kubo, Kazuihiro, Shizuoka, Japan Karasawa, Akira, Huntingdon Valley, PA, United States Ohno, Tetsuji, Shizuoka, Japan Shiozaki, Shizuo, Fuji, Japan Ishii, Akio, Shizuoka, Japan Shuto, Katsuichi, Mishima, Japan
PATENT ASSIGNEE(S):	Kyowa Hakko Kogyo Co., Ltd., Tokyo, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5173492		19921222
APPLICATION INFO.:	US 1991-752180		19910823 (7)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1990-581562, filed on 12 Sep 1990, now abandoned		

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1989-239117	19890914
	JP 1989-261761	19891006

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Bond, Robert T.
ASSISTANT EXAMINER:	Gupta, Y. N.
LEGAL REPRESENTATIVE:	Fitzpatrick, Cella, Harper & Scinto
NUMBER OF CLAIMS:	10
EXEMPLARY CLAIM:	1
LINE COUNT:	2150

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB There are disclosed s-triazolo[3,4-i]purine derivatives represented by formula: ##STR1## wherein Y-Z represents ##STR2## R.sub.4 represents hydrogen, alkyl, substituted or unsubstituted aromatic heterocyclic group or substituted or unsubstituted aryl; and X.sup.2 represents oxygen, sulfur or NH; each of R.sup.1 and R.sup.2 independently represents hydrogen, alkyl, cycloalkyl, aralkyl or substituted or unsubstituted aryl; R.sup.3 represents alkyl, cycloalkyl, aralkyl or substituted or unsubstituted aryl; X.sup.1 represents oxygen or sulfur; and represents a single bond or a double bond or pharmaceutically acceptable salts thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 24 OF 28 USPATFULL on STN

ACCESSION NUMBER:	92:5575 USPATFULL
TITLE:	Therapeutic xanthine derivatives for the treatment of peptic ulcer disease
INVENTOR(S):	Wolf, Erhard, Hofheim am Taunus, Germany, Federal Republic of Gebert, Ulrich, Kelkheim, Germany, Federal Republic of Furrer, Harald, Kelkheim, Germany, Federal Republic of Tanaka, Toshizo, Saitama, Japan Sakurai, Masao, Saitama, Japan Goto, Masayoshi, Kanagawa, Japan
PATENT ASSIGNEE(S):	Hoechst Japan Limited, Tokyo, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5082845		19920121

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1988-35484	19880219

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Rivers, Diana G.
LEGAL REPRESENTATIVE: Finnegan, Henderson, Farabow, Garrett, and Dunner
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1,5
LINE COUNT: 572
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Therapeutic agents for the treatment of peptic ulcer disease, containing as active ingredient, at least one compound of the general formula ##STR1## wherein R.sup.1 and R.sup.3 are the same or different and are each (C.sub.1 -C.sub.8)alkyl, ##STR2## R.sup.2 is (C.sub.1 -C.sub.4)alkyl; R.sup.4 and R.sup.5 are the same or different and are each hydrogen or (C.sub.1 -C.sub.2)alkyl; R.sup.6 is (C.sub.1 -C.sub.2)alkyl; and m, n and p are the same or different and are each 1, 2, 3, 4, 5 or 6; with the proviso that one of the groups R.sup.1 and R.sup.3 is ##STR3## or that R.sup.3 represents ##STR4## Some of the compounds of formula I are novel.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 25 OF 28 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 91275356 MEDLINE
DOCUMENT NUMBER: 91275356 PubMed ID: 1647281
TITLE: Inhibition of cyclic GMP phosphodiesterase by xanthine derivatives relaxes guinea-pig trachealis smooth muscle.
AUTHOR: Tanaka H; Ogawa K; Takagi K; Satake T; Hidaka H
CORPORATE SOURCE: Second Department of Internal Medicine, Nagoya University School of Medicine, Japan.
SOURCE: CLINICAL AND EXPERIMENTAL PHARMACOLOGY AND PHYSIOLOGY, (1991 Mar) 18 (3) 163-8.
Journal code: 0425076. ISSN: 0305-1870.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199107
ENTRY DATE: Entered STN: 19910818
Last Updated on STN: 19970203
Entered Medline: 19910729
AB 1. For the purpose of clarifying the mechanism of the airways smooth muscle relaxant action of xanthines, cyclic guanosine monophosphate (GMP) phosphodiesterase (PDE) from guinea-pig trachealis muscle was purified with diethylaminoethyl ether (DEAE) cellulose column chromatography. 2. Five 3-alkylxanthines (3-methylxanthine, 3-ethylxanthine, ***3*** - ***n*** - ***propylxanthine*** (enprofylline), 3-n-butylxanthine, and 3-iso-butylxanthine), and five 1-methyl-3-alkylxanthines (1-methyl-3-methyl-xanthine (theophylline), 1-methyl-3-ethylxanthine, 1-methyl- ***3*** - ***n*** - ***propylxanthine*** , 1-methyl-3-n-butylxanthine, and 1-methyl-3-iso-butylxanthine (IBMX] were compared in terms of purified cyclic GMP PDE inhibition. The relationship between the structure and inhibition of cyclic GMP PDE was studied. 3. The -log EC50 values for relaxation of spontaneous tone of isolated guinea-pig trachealis preparations by the 3-alkylxanthines and 1-methyl-3-alkylxanthines were determined. 4. The five 1-methyl-3-alkylxanthines were each more potent in relaxing isolated trachealis smooth muscle than the corresponding 3-alkylxanthines. The 1-methyl-3-alkylxanthines were also more potent than the corresponding 3-alkylxanthines in their cyclic GMP PDE inhibitory effect. There was a strong positive correlation between the concentration of inhibitor which inhibited hydrolysis by 50% (IC50) values for cyclic GMP PDE inhibition by the xanthine derivatives and their EC50 values for trachealis muscle relaxation. 5. It is suggested that the mechanism by which xanthine derivatives relax trachealis smooth muscle involves inhibition of cyclic GMP PDE in addition to inhibition of cyclic adenosine monophosphate PDE.

L6 ANSWER 26 OF 28 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 89336274 MEDLINE
DOCUMENT NUMBER: 89336274 PubMed ID: 2547475
TITLE: Mechanism of xanthine-induced relaxation of guinea-pig isolated trachealis muscle.
AUTHOR: Ogawa K; Takagi K; Satake T

Nagoya University, Japan.
OURCE: BRITISH JOURNAL OF PHARMACOLOGY, (1989 Jun) 97 (2) 542-6.
Journal code: 7502536. ISSN: 0007-1188.
UB. COUNTRY: ENGLAND: United Kingdom
OCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
ANGUAGE: English
ILE SEGMENT: Priority Journals
NTRY MONTH: 198909
NTRY DATE: Entered STN: 19900309
Last Updated on STN: 19900309
Entered Medline: 19890921

B 1. Four 3-alkylxanthines (3-methylxanthine, ***3*** - ***n*** - ***propylxanthine*** (enprofylline), 3-n-butylxanthine and 3-iso-butylxanthine) and four 1-methyl-3-alkylxanthines (1-methyl-3-methylxanthine (theophylline), 1-methyl- ***3*** - ***n*** - ***propylxanthine*** , 1-methyl-3-n-butylxanthine and 1-methyl-3-iso-butylxanthine (IBMX], were compared in terms of cyclic AMP phosphodiesterase (PDE) inhibition and trachealis muscle relaxation. The relationship between xanthine structure and cyclic AMP PDE inhibition was also studied. 2. Xanthine induced relaxation of guinea-pig isolated trachealis muscle was measured against spontaneous tone. 3. The four 1-methyl-3-alkylxanthines were each significantly more potent than the corresponding 3-alkylxanthines in relaxing the isolated trachealis muscle. The 1-methyl-3-alkylxanthines were similarly more potent than the corresponding 3-alkyl derivatives in inhibiting low Km cyclic AMP PDE. There was a strong positive correlation between low Km cyclic AMP PDE inhibition and the tracheal smooth muscle relaxation evoked by the xanthine derivatives. 4. Since methylation of the 1-position of each 3-alkylxanthine increased the potency of the derivative in inhibiting low Km cyclic AMP PDE and in relaxing trachealis muscle and since a strong positive correlation was observed between the relaxant EC50 and the Ki value of each xanthine derivative, it is suggested that low Km cyclic AMP PDE inhibition by xanthines plays an important role in their tracheal relaxant effect.

6 ANSWER 27 OF 28 USPATFULL on STN
CCESSION NUMBER: 88:72477 USPATFULL
ITLE: 8-arylxanthines
NVENTOR(S): Rzeszotarski, Waclaw J., Millersville, MD, United States
Hicks, Rickey P., Columbia, MD, United States
Erickson, Ronald H., Baltimore, MD, United States
ATENT ASSIGNEE(S): Marion Laboratories, Inc., Kansas City, MO, United States (U.S. corporation)

	NUMBER	KIND	DATE
ATENT INFORMATION:	US 4783530		19881108
PPLICATION INFO.:	US 1987-108990		19871001 (7)

ELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1986-931620, filed on 13 Nov 1986, now abandoned
OCUMENT TYPE: Utility
ILE SEGMENT: Granted
RIMARY EXAMINER: Rizzo, Nicholas S.
EGAL REPRESENTATIVE: Dewey, Ballantine, Busby, Palmer & Wood
UMBER OF CLAIMS: 8
XEMPLARY CLAIM: 1
INE COUNT: 705
AS INDEXING IS AVAILABLE FOR THIS PATENT.
B 1,3-alkylsubstituted-8-(3,4-,3- or 4-substituted phenyl)xanthines and pharmaceutically acceptable salts of such compounds are disclosed. The 3-substituents are hydrogen, dimethylaminomethyl, or 2,3-dihydroxypropyloxy. The 4-substituents are selected from hydroxy, cyano, --NHCON(R.sub.5).sub.2, --C(.dbd.NH)N(R.sub.5).sub.2, --NH--C(.dbd.NH)N(R.sub.5).sub.2, with each R.sub.5 independently being hydrogen or an alkyl group of one to three carbons and provided that when the 3-substituent is hydrogen the 4-substituent is not hydroxy or hydrogen.

The compounds are potent adenosine receptor antagonists having relatively low lipophilicity. The compounds are intended for use as bronchodilators and cardiotonics.

AS INDEXING IS AVAILABLE FOR THIS PATENT.

6 ANSWER 28 OF 28 USPATFULL on STN

TLE: Xanthine compounds and method of treating bronchospastic and allergic diseases
VENTOR(S): Diamond, Julius, Morris Plains, NJ, United States
TENT ASSIGNEE(S): Cooper Laboratories, Inc., Parsippany, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
TENT INFORMATION:	US 4120947		19781017
PLICATION INFO.:	US 1976-672388		19760331 (5)

CUMENT TYPE: Utility
LE SEGMENT: Granted
IMARY EXAMINER: Schenkman, Leonard
GAL REPRESENTATIVE: Kolano, John J., Boland, Thomas R.
MBER OF CLAIMS: 48
EMPLARY CLAIM: 1,16
NE COUNT: 1360
S INDEXING IS AVAILABLE FOR THIS PATENT.

Bronchial asthma and other bronchospastic and allergic diseases are treated by administering an effective amount of a substituted xanthine compound having the formula: ##STR1## wherein: R.sub.1 = C.sub.1 -C.sub.3 alkyl,

R.sub.3 = c.sub.1 -c.sub.7 alkyl, C.sub.3 -C.sub.7 alkenyl, C.sub.3 -C.sub.7 alkynyl, C.sub.3 -C.sub.7 cycloalkyl or C.sub.4 -C.sub.7 cycloalkylalkyl,

R.sub.8 = h, c.sub.1 -c.sub.4 alkyl, C.sub.3 -C.sub.4 alkenyl, C.sub.3 -C.sub.4 alkynyl or C.sub.3 -C.sub.4 cycloalkyl,

R = c.sub.1 -c.sub.4 alkyl, 2-halo C.sub.2 -C.sub.3 alkyl, or phenyl

Novel and preferred bronchodilator and antiallergy compounds are disclosed having the formula ##STR2## wherein: R.sub.1 = C.sub.1 -C.sub.2 alkyl

R.sub.3 = ch.sub.2 --(c.sub.3 -c.sub.4 alkyl),--CH.sub.2 --(C.sub.3 -C.sub.4 alkenyl), or --CH.sub.2 --(C.sub.3 -C.sub.4 cycloalkyl)

R.sub.8 = h, c.sub.1 -c.sub.2 alkyl,

R = c.sub.1 -c.sub.4 alkyl, 2-halo C.sub.2 -C.sub.3 alkyl, or phenyl

The bronchodilator and antiallergy agents may be administered in the form of tablets, capsules or aerosols.

S INDEXING IS AVAILABLE FOR THIS PATENT.

ecuting the logoff script...

LOG H

ST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
LL ESTIMATED COST	95.93	96.14

SCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
SUBSCRIBER PRICE	-0.69	-0.69

ESSION WILL BE HELD FOR 60 MINUTES
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GINID:ssspta1635kxh

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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


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 NEWS  2          "Ask CAS" for self-help around the clock
 NEWS  3  SEP 09  CA/CAplus records now contain indexing from 1907 to the
                  present
 NEWS  4  DEC 08  INPADOC: Legal Status data reloaded
 NEWS  5  SEP 29  DISSABS now available on STN
 NEWS  6  OCT 10  PCTFULL: Two new display fields added
 NEWS  7  OCT 21  BIOSIS file reloaded and enhanced
 NEWS  8  OCT 28  BIOSIS file segment of TOXCENTER reloaded and enhanced
 NEWS  9  NOV 24  MSDS-CCOHS file reloaded
 NEWS 10  DEC 08  CABA reloaded with left truncation
 NEWS 11  DEC 08  IMS file names changed
 NEWS 12  DEC 09  Experimental property data collected by CAS now available
                  in REGISTRY
 NEWS 13  DEC 09  STN Entry Date available for display in REGISTRY and CA/CAplus
 NEWS 14  DEC 17  DGENE: Two new display fields added
 NEWS 15  DEC 18  BIOTECHNO no longer updated
 NEWS 16  DEC 19  CROPU no longer updated; subscriber discount no longer
                  available
 NEWS 17  DEC 22  Additional INPI reactions and pre-1907 documents added to CAS
                  databases
 NEWS 18  DEC 22  IFIPAT/IFIUDB/IFICDB reloaded with new data and search fields
 NEWS 19  DEC 22  ABI-INFORM now available on STN

 NEWS EXPRESS  DECEMBER 28 CURRENT WINDOWS VERSION IS V7.00, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 23 SEPTEMBER 2003
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 NEWS WWW      CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 14:32:04 ON 21 JAN 2004

=> b medline
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'MEDLINE' ENTERED AT 14:32:14 ON 21 JAN 2004

 FILE LAST UPDATED: 20 JAN 2004 (20040120/UP).  FILE COVERS 1958 TO DATE.

 On December 14, 2003, the 2004 MeSH terms were loaded.  See HELP RLOAD
 for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2004 vocabulary.  See http://www.nlm.nih.gov/mesh/ and
 http:\\www.nih.gov/pubs/yechbull/nd03/nd03_mesh.html for a description
 on changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> s adenosine receptor a.sub.2b
        139950 ADENOSINE
        445191 RECEPTOR
       7408560 A
```

```
        13946 2B
L1          0 ADENOSINE RECEPTOR A.SUB.2B
              (ADENOSINE(W)RECEPTOR(W)A(W)SUB(W)2B)

=> s adenosine receptor a2b
       139950 ADENOSINE
       445191 RECEPTOR
          477 A2B
L2          2 ADENOSINE RECEPTOR A2B
              (ADENOSINE(W)RECEPTOR(W)A2B)

=> d l2 ibib abs tot

L2   ANSWER 1 OF 2     MEDLINE on STN
ACCESSION NUMBER:   2003026586     MEDLINE
DOCUMENT NUMBER:    22387572   PubMed ID: 12500024
TITLE:              Adenosine receptor subtypes mediating coronary vasodilation
                    in rat hearts.
AUTHOR:             Hinschen Andrea K; Rose'Meyer Roselyn B; Headrick John P
CORPORATE SOURCE:   Heart Foundation Research Center, School of Health Science,
                    Griffith University Gold Coast Campus, Southport, QLD 4215,
                    Australia.
SOURCE:             JOURNAL OF CARDIOVASCULAR PHARMACOLOGY, (2003 Jan) 41 (1)
                    73-80.
                    Journal code: 7902492. ISSN: 0160-2446.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200306
ENTRY DATE:         Entered STN: 20030122
                    Last Updated on STN: 20030604
                    Entered Medline: 20030603
AB   Adenosine receptor-mediated coronary vasodilation was studied in isolated
     hearts from young (1-2 months) and mature (12-18 months) Wistar rats.  The
     nonselective agonist 5'-N-ethylcarboxamidoadenosine (NECA) induced
     biphasic concentration-dependant dilation with similar potencies in both
     age groups (p < 0.05).  Despite similar potencies, responses to NECA were
     significantly depressed by 50% with age.  NECA-mediated dilation was
     unaltered by selective A adenosine receptor (A1AR) antagonist
     1,3-dipropyl-8-cyclopentylxanthine (DPCPX, 100 nM ) or A adenosine
     receptor (A2AAR) antagonist 5-amino-7-(2-phenylethyl)-2-(2-furyl)-pyrazolo-
     [4,3-e]-1,2,4-triazolo[1,5- ]pyrimidine (SCH 58261, 100 nM ).  However,
     the A2B   ***adenosine***     ***receptor***   (  ***A2B***   AR)
     selective antagonist alloxazine (10 microM ) significantly reduced
     response magnitude to NECA in both age groups.  Concentration-response
     curves to N -2-(4-aminophenyl) ethyladenosine (APNEA) induced biphasic
     concentration-dependent dilation in hearts from young animals.  In the
     presence of the three combined antagonists, 1 microM DPCPX, 100 nM SCH
     58261, and 1 microM alloxazine, the response magnitude was significantly
     attenuated (p < 0.05).  The addition of the A3 adenosine receptor (A3AR)
     antagonist 3-ethyl-5-benzyl-2-methyl-4-phenylethyl-6-phenyl-1,4-(+/-)-
     dihydropyridine-3,5-dicarboxylate (MRS1191, 100 nM ) to the combined
     antagonists further attenuated vasodilator responses to APNEA.  The
     results suggest that multiple adenosine receptor subtypes mediate dilation
     in the rat coronary circulation.  NECA mediates vasodilation via the A2BAR
     subtype, while dilator responses to APNEA in the presence and absence of
     A1, A2, and A3 ARs antagonists provide evidence for a vasodilator role for
     A3 ARs in rat coronary circulation.  The magnitude of the coronary dilator
     response is reduced with age and does not involve A2A or A1 ARs.

L2   ANSWER 2 OF 2     MEDLINE on STN
ACCESSION NUMBER:   2002353022     MEDLINE
DOCUMENT NUMBER:    22091032   PubMed ID: 12096342
TITLE:              Identification and characterization of the Myb-inducible
                    promoter of the chicken adenosine receptor 2B gene.
AUTHOR:             Kattmann Dana; Klempnauer Karl-Heinz
CORPORATE SOURCE:   Institut fur Biochemie, Westfalische-Wilhelms-Universitat
                    Munster, Wilhelm-Klemm-Str. 2, D-48149 Munster, Germany.
SOURCE:             ONCOGENE, (2002 Jul 11) 21 (30) 4663-72.
                    Journal code: 8711562. ISSN: 0950-9232.
PUB. COUNTRY:       England: United Kingdom
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
OTHER SOURCE:       GENBANK-AF508797
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ENTRY DATE:          Entered STN: 20020704
                     Last Updated on STN: 20020801
                     Entered Medline: 20020731
AB   Numerous studies have shown that the retroviral oncogene v-myb encodes a
     transcription factor (v-Myb) which interferes with the differentiation
     program of myelomonocytic cells.  It is generally thought that v-Myb
     deregulates the expression of specific target genes and thereby causes
     transformation of these cells.  By using an estrogen-inducible version of
     v-Myb we have previously identified the gene for the chicken A2B
       ***adenosine***     ***receptor***   (  ***A2B***  -AR), a member of the
     seven-pass transmembrane receptor superfamily, as a bona fide target gene
     for v-Myb.  The chicken A2B-AR gene is expressed in v-myb transformed
     myeloblasts as well as in c-myb expressing erythroblasts, offering the
     opportunity to study how Myb transcription factors activate a target gene
     in two different hematopoietic lineages.  Here, we report the
     characterization of the promoter of the A2B-AR gene.  We show that the
     A2B-AR promoter region contains an exceptionally large number of Myb
     binding sites, many of which contribute to the Myb-inducibility of the
     promoter.  The same sites were required for promoter activity in
     myelomonocytic and erythroid cells.  In contrast to the promoters of other
     Myb target genes the A2B-AR promoter was not activated synergistically by
     Myb and other lineage-specific transcription factors that have been
     identified as Myb cooperation partners before.  Taken together, our data
     suggest that the activation of the A2B-AR promoter by Myb depends on the
     simultaneous binding of a large number of Myb molecules.


=> s adenosine receptor agonist
        139950 ADENOSINE
        445191 RECEPTOR
         80450 AGONIST
L3         441 ADENOSINE RECEPTOR AGONIST
                 (ADENOSINE(W)RECEPTOR(W)AGONIST)

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4          441 DUP REM L3 (0 DUPLICATES REMOVED)

=> s l4 and py<2000
L5          441 S L4
      11603593 PY<2000
L6          348 L5 AND PY<2000

=> s l6 and a()b
       7408560 A
        559675 B
         29189 A(W)B
L7           0 L6 AND A(W)B

=> d l6 kwic 1-10

L6   ANSWER 1 OF 348     MEDLINE on STN
SO   JOURNAL OF HYPERTENSION,   ***(1996 Jan)***   14 (1) 75-9.
     Journal code: 8306882. ISSN: 0263-6352.
AB   OBJECTIVE: We studied the dose-response effects of acute administration of
     the selective A1   ***adenosine***     ***receptor***     ***agonist***
     2-chloro-N6-cyclopentyladenosine (CCPA), the selective A2A agonists
     2-hexynyl-5'-N-ethylcarboxamidoadenosine (2HE-NECA) and
     2-[4-(2-carboxyethyl)phenethylamino]-5'-N-ethylcarboxamidoadenosine (CGS
     21680) and the non-selective agonist N-ethylcarboxamidoadenosine (NECA) on
     plasma.  .  .

L6   ANSWER 2 OF 348     MEDLINE on STN
SO   MOLECULAR REPRODUCTION AND DEVELOPMENT,   ***(1999 Aug)***   53 (4)
     459-71.
     Journal code: 8903333. ISSN: 1040-452X.
AB   .  .  .  to adenosine, especially in capacitated suspensions, consistent
     with interaction between FPP and adenosine receptors.  CGS-21680 (1
     microM), a stimulatory A2a   ***adenosine***     ***receptor***
       ***agonist***  , significantly stimulated capacitation and cAMP in
     uncapacitated cells, while cyclopentyl adenosine (1 microM), an inhibitory
     A1   ***adenosine***     ***receptor***     ***agonist***   only affected
     capacitated cells, inhibiting spontaneous acrosome loss.  Responses to FPP
     and adenosine were inhibited in uncapacitated cells by a.  .  .

L6   ANSWER 3 OF 348     MEDLINE on STN
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Journal code: 8006226. ISSN: 0143-4160.
AB . . . monitored. Con-A mimicked the response induced by antigen, whilst A23187 and thapsigargin induced a large transient non-oscillatory response. NECA, an ***adenosine*** ***receptor*** ***agonist*** , induced only a small transient rise in Ca2+[i without oscillatory behaviour. Since all these stimuli accept NECA-induced degranulation in these. . .

L6 ANSWER 4 OF 348 MEDLINE on STN
SO JOURNAL OF BASIC AND CLINICAL PHYSIOLOGY AND PHARMACOLOGY, ***(1999)*** 10 (4) 287-303.
Journal code: 9101750. ISSN: 0792-6855.
AB The present study demonstrates that: a) adenosine and R-N6-(2-phenylisopropyl)-adenosine (R-PIA, A1 and A3 ***adenosine*** ***receptor*** ***agonist***) inhibited [3H]deoxyglucose uptake or [3H]3-O-methyl-D-glucose uptake; b) sugar uptake reflects the rate of contraction in cardiac cultures; c) [3H]deoxyglucose uptake. . .

L6 ANSWER 5 OF 348 MEDLINE on STN
SO MOLECULAR AND CELLULAR ENDOCRINOLOGY, ***(1999 Nov 25)*** 157 (1-2) 31-9.
Journal code: 7500844. ISSN: 0303-7207.
AB . . . levels is transcriptional. The stimulatory effect of adenosine on NIS mRNA levels, is mimicked by N6-(L-2-phenylisopropyl) adenosine (PIA), an A1 ***adenosine*** ***receptor*** ***agonist*** , and inhibited by 1,3-dipropyl-8-cyclopentylxanthine, an A1 adenosine receptor antagonist, suggesting that the effect is mediated via the A1 adenosine receptor. . .

L6 ANSWER 6 OF 348 MEDLINE on STN
SO BRITISH JOURNAL OF PHARMACOLOGY, ***(1999 Dec)*** 128 (7) 1623-9.
Journal code: 7502536. ISSN: 0007-1188.
AB 1. Adenosine and the A1- ***adenosine*** ***receptor*** ***agonist*** R-PIA, exerted a negative inotropic effect in isolated, electrically driven left atria of wild-type mice. 2. In left atria of. . .

L6 ANSWER 7 OF 348 MEDLINE on STN
SO EUROPEAN JOURNAL OF PHARMACOLOGY, ***(1999 Oct 27)*** 383 (2) 143-53.
Journal code: 1254354. ISSN: 0014-2999.
AB The rate of onset of the negative inotropic responses of guinea-pig isolated paced atria to the ***adenosine*** ***receptor*** ***agonist*** , N(6)-cyclopentyladenosine, was significantly slowed by the K(+) channel inhibitor, 4-aminopyridine (10 mM). The concentration-dependent inhibition of developed tension by N(6)-cyclopentyladenosine,. . .

L6 ANSWER 8 OF 348 MEDLINE on STN
SO EUROPEAN JOURNAL OF NEUROSCIENCE, ***(1999 Oct)*** 11 (10) 3617-25.
Journal code: 8918110. ISSN: 0953-816X.
AB . . . CA3. MHC class II antigen was also detected in the regions of c-Jun phosphorylation. Coadministration of N6-cyclopenthyladenosine (CHA), an A1 ***adenosine*** ***receptor*** ***agonist*** , attenuated the neuronal cell loss in the CA1 and CA3 with or without pretreatment with CPT. These results strongly suggest. . .

L6 ANSWER 9 OF 348 MEDLINE on STN
SO JOURNAL OF PHYSIOLOGY, ***(1999 Nov 15)*** 521 Pt 1 81-97.
Journal code: 0266262. ISSN: 0022-3751.
AB . . . IAC by a maximum of 78.4 +/- 4.6 % (n = 8) with an IC50 of 71 nM. The non-selective ***adenosine*** ***receptor*** ***agonist*** NECA effectively inhibited IAC by 79.3 +/- 2.9 % (n = 24) at a concentration of 100 nM. 2. Inhibition. . .

L6 ANSWER 10 OF 348 MEDLINE on STN
SO APMIS, ***(1999 Oct)*** 107 (10) 896-902.
Journal code: 8803400. ISSN: 0903-4641.
AB . . . murine T-cell development was evaluated by culturing day 15-16 fetal thymic lobes in the presence of various concentrations of the ***adenosine*** ***receptor*** ***agonist*** 5'-(N-ethyl)-carboxamidoadenosine (NECA) or the adenosine receptor antagonist 8-phenyl-theophylline (8-PT) using the fetal thymic organ culture (FTOC) system. Before and 8. . .

=> s l6 and a2

L8 108 L6 AND A2

=> d l8 kwic 1-10

L8 ANSWER 1 OF 108 MEDLINE on STN
TI Selective reduction in ***A2*** adenosine receptor desensitization following antisense-induced suppression of G protein-coupled receptor kinase 2 expression.
SO JOURNAL OF NEUROCHEMISTRY, ***(1999 Nov)*** 73 (5) 1781-9.
Journal code: 2985190R. ISSN: 0022-3042.
AB . . . play a critical role in the desensitization of responses mediated by these receptors. To explore the role of GRK2 in ***A2*** adenosine receptor desensitization, we attempted to reduce specifically GRK2 expression in NG108-15 cells by stable transfection with an antisense rat. . . promote light-dependent phosphorylation of rhodopsin. Levels of GRK3 were the same in antisense and plasmid-transfected controls. On addition of the ***A2*** ***adenosine*** ***receptor*** ***agonist*** 5'-(N-ethylcarboxamido)adenosine, cyclic AMP accumulation was greater in GRK2 antisense cells as compared with plasmid control cells. In contrast, cyclic AMP. . . IP-prostanoid or secretin receptors or by addition of forskolin was not significantly different among all clones examined. The increase in ***A2*** adenosine receptor response could not be explained by changes in A2A adenosine receptor expression, as assessed by ligand binding experiments. . . ([3H]ZM241385). These data show for the first time a direct correlation between expression of GRK2 and desensitization of natively expressed ***A2*** adenosine receptors in intact cells, suggesting that GRK2 plays a major role in the regulation of these receptors. Key Words: G protein-coupled receptor kinase-G protein-coupled receptor-Antisense-NG108-15 cells- ***A2*** adenosine receptors-Desensitization.

L8 ANSWER 2 OF 108 MEDLINE on STN
SO CLINICAL AND EXPERIMENTAL PHARMACOLOGY AND PHYSIOLOGY, ***(1999*** *** May-Jun)*** 26 (5-6) 438-43.
Journal code: 0425076. ISSN: 0305-1870.
AB . . . of preconstriction on the responses to adenosine analogues were examined in the present study. 2. Relaxation responses to the non-selective ***adenosine*** ***receptor*** ***agonist*** N-ethylcarboxamidoadenosine (NECA) were endothelium independent. N-Ethylcarboxamidoadenosine, GR 79236 (A1 receptor selective) and 8-cyclopentyl-1,3-dipropylxanthine (CGS 21680) (A2A receptor selective) produced full. . . potency was CGS 21680 = NECA > GR 79236, consistent with that defining the A2A receptor subtype. 3. 3,7-Dimethyl-1-propargylxanthine (DMPX; ***A2*** receptor selective) competitively antagonized NECA and CGS 21680 with pKB values of 4.95 +/- 0.09 and 5.06 +/- 0.22, respectively.. . .

L8 ANSWER 3 OF 108 MEDLINE on STN
SO AMERICAN JOURNAL OF PHYSIOLOGY, ***(1999 Jun)*** 276 (6 Pt 2) H1877-83.
Journal code: 0370511. ISSN: 0002-9513.
AB The adenosine agonist 5-(N-ethylcarboxamido)adenosine (NECA) induces vasodilation in the pulmonary circulation via ***A2*** -adenosine-receptor activation. We addressed whether prolonged treatment with NECA desensitizes in ***A2*** -adenosine- receptor function in isolated lung and pulmonary artery smooth muscle cells (PASMC). In lung microcirculation preconstricted with a hypoxic gas,. . . in cholera toxin-treated NECA-desensitized PASMCs compared with cholera toxin-treated control PASMCs, demonstrating that Gsalpha-adenylyl cyclase signaling contributes to desensitization. The A2a- ***adenosine*** - ***receptor*** ***agonist*** CGS-21680C neither increased cAMP accumulation in PASMCs nor attenuated NECA-induced vasodilation. These data support that the A2b-adenosine receptor is responsible. . .

L8 ANSWER 4 OF 108 MEDLINE on STN
SO JOURNAL OF NEUROPHYSIOLOGY, ***(1999 Jan)*** 81 (1) 247-55.
Journal code: 0375404. ISSN: 0022-3077.
AB . . . inhibited the respiratory rhythm. This was accompanied by increase in the activity of KATP channels in cell-attached patches. The A1 ***adenosine*** ***receptor*** ***agonist*** , 2-chloro-N6-cyclopentyladenosine (CCPA, 0.3-2 microM), inhibited the respiratory rhythm, sPSCs, and enhanced activity of KATP channels. The A1 adenosine receptor antagonist, 8-cyclopentyl-1, 3-dipropylxanthine (DPCPX, 1-3 microM), showed opposite effects and occluded the CCPA actions. Agents specific for ***A2*** adenosine receptors (CGS 21860 and NECA, both applied at 1-10 microM) were without effect. Elevation of

ANSWER 5 OF 108 MEDLINE on STN
JOURNAL OF SURGICAL RESEARCH, ***(1998 Dec)*** 80 (2) 357-64.
Journal code: 0376340. ISSN: 0022-4804.
. . . determine whether adenosine also enhances NO production from human arterial endothelium and to define the involvement of adenosine A1 and ***A2*** receptors. MATERIALS AND METHODS. Human iliac arterial endothelial cells (HIAEC) and PCAEC were harvested and cultured in dishes. NO production. . . NO content of the medium bathing HIAEC and PCAEC was significantly increased with adenosine (100 micromol/L). Ethylcarboxamidoadenosine (NECA), a nonselective ***adenosine*** ***receptor*** ***agonist*** , and carboxyethyl-phenethylamino-ethylcarboxamidoadenosine (CGS-21680), a selective adenosine A2a receptor agonist, increased NO production by HIAEC and PCAEC with respective EC50 values. . . and 6.96 nmol/L for NECA and 30.97 and 29.47 nmol/L for CGS-21680. Chlorofuryl-triazolo-quinazolinamine (CGS-15943; 1 micromol/L), an adenosine A1 and ***A2*** receptor antagonist, and aminofuryltriazolotriazinyl-aminoethylphenol (ZM-241385; 1 micromol/L), a selective adenosine A2a receptor antagonist, inhibited the effect of CGS-21680. Chlorocyclopentyl-adenosine (CCPA;. . .

ANSWER 6 OF 108 MEDLINE on STN
AMERICAN JOURNAL OF PHYSIOLOGY, ***(1998 Nov)*** 275 (5 Pt 1) L990-7.
Journal code: 0370511. ISSN: 0002-9513.
. . . A1 adenosine receptor in airway smooth muscle from allergic rabbits was studied by investigating the effect of the selective A1 ***adenosine*** - ***receptor*** ***agonist*** N6-cyclopentyladenosine (CPA) on tissue levels of inositol 1,4, 5-trisphosphate [Ins(1,4,5)P3] measured by protein binding assay. CPA caused a rapid, transient,. . . the adenosine-receptor antagonist 8-(p-sulfophenyl)-theophylline, suggesting that the effect was mediated by A1 adenosine receptors. On the other hand, the ***A2*** ***adenosine*** - ***receptor*** ***agonist*** CGS-21680 was ineffective in altering the tissue concentration of Ins(1,4,5)P3, indicating that ***A2*** adenosine receptors may not be involved in the activation of PLC in the allergic rabbit airway smooth muscle. In this. . .

ANSWER 7 OF 108 MEDLINE on STN
A1 and ***A2*** adenosine receptor modulation of contractility in the cauda epididymis of the guinea-pig.
BRITISH JOURNAL OF PHARMACOLOGY, ***(1998 Oct)*** 125 (3) 570-6.
Journal code: 7502536. ISSN: 0007-1188.
. . . from preparations of epididymis. In the absence or presence of the L-type Ca2+ channel blocker, nifedipine (10 microM) the non-selective ***adenosine*** ***receptor*** ***agonist*** , 5'-N-ethylcarboxamidoadenosine (NECA, 1 microM) shifted phenylephrine concentration-response curves to the left (4 and 5 fold respectively). Following the incubation of. . . 241385 (apparent pKB 8.60+/-0.76). 5. These studies are consistent with the action of stable adenosine analogues at post-junctional A1 and ***A2*** adenosine receptors in the epididymis of the guinea-pig. A1 Adenosine receptors potentiate alpha1-adrenoceptor contractility, an effect blocked by pertussis toxin, but which may not be dependent upon an inhibition of adenylyl cyclase. The epididymis of the guinea-pig also contains ***A2*** adenosine receptors, possibly of the A2A subtype, which both inhibit contractility and also stimulate adenylyl cyclase.

ANSWER 8 OF 108 MEDLINE on STN
BRITISH JOURNAL OF PHARMACOLOGY, ***(1998 Sep)*** 125 (2) 379-87.
Journal code: 7502536. ISSN: 0007-1188.
. . . of pro-and anti-inflammatory cytokines. Here we evaluated the effect of adenosine and various ligands of the adenosine receptor subtypes (A1, ***A2*** , A3) on the chemokine macrophage inflammatory protein (MIP) 1alpha production in immunostimulated RAW macrophages in vitro. Furthermore, we studied whether a selected A3 ***adenosine*** ***receptor*** ***agonist*** inhibits MIP-1alpha production and affects the course of inflammation in collagen-induced arthritis. 2. In the cultured macrophages, the A3 receptor agonist N6-(3-iodobenzyl)-adenosine-5'-N-methyluronamide (IB-MECA), and, less potently, the ***A2*** receptor agonist 2-p-(2-carboxyethyl) phenethylamino-5'-N-ethyl-carboxamidoadenosine (CGS; 1-200 micro) dose-dependently suppressed the production of MIP-1alpha. The selective A1 receptor agonist 2-chloro-N6-cyclopentyladenosine (CCPA, 1-200 microM) was ineffective, and adenosine was a weak inhibitor. The inhibition of MIP-1alpha production by the A3 and ***A2*** agonist was associated with suppression of its

that activation of A3, and to a lesser extent ***A2*** adenosine receptors suppresses MIP-1alpha expression. Since IB-MECA was the most potent inhibitor of MIP-1alpha expression, we next investigated whether it. . . A3 agonist IB-MECA suppress the production of MIP-alpha, and exert anti-inflammatory effects. Therefore, stimulation of adenosine receptor subtypes A3 and ***A2*** may be a strategy worthy of further evaluation for the abrogation of acute or chronic inflammatory disorders.

L8 ANSWER 9 OF 108 MEDLINE on STN
SO BRITISH JOURNAL OF PHARMACOLOGY, ***(1998 Sep)*** 125 (2) 347-56.
Journal code: 7502536. ISSN: 0007-1188.
AB . . . forskolin was the same in GRK2 overexpressing cells and plasmid-transfected control cells. 3. Cells overexpressing GRK2 were more sensitive to ***adenosine*** ***receptor*** ***agonist*** -induced desensitization than plasmid-transfected control cells. This effect was selective since the agonist sensitivity of desensitization for secretin and IP-prostanoid receptor-stimulated. . . cyclase activity was not affected by GRK2 overexpression. 4. These results further implicate GRK2 as the likely mechanism by which ***A2*** adenosine receptors undergo short-term desensitization in NG108-15 cells, and indicate that even when overexpressed, GRK2 retains its substrate specificity for. . .

L8 ANSWER 10 OF 108 MEDLINE on STN
SO PROCEEDINGS OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE, ***(1998 Sep)*** 218 (4) 341-8.
Journal code: 7505892. ISSN: 0037-9727.
AB . . . of 10-100 microM. This effect was not mimicked by adenosine metabolites adenine, hypoxanthine, or inosine. N-ethylcarboxamidoadenosine (NECA, a relatively nonselective ***adenosine*** ***receptor*** ***agonist***) and 2-p-(2-carboxyethyl) phenethylamino-5'-N ethylcarbox-amidoadenosine (CGS-21680, an ***A2*** selective agonist) also increased DNA synthesis by mammary epithelial cells. However, N6-cyclohexyladenosine (CHA, an agonist for A1 type receptors) decreased DNA synthesis. The A1 selective antagonist 8-cyclopentyl-1,3-dipropylxanthine (DPCPX) had no effect on basal or adenosine-induced DNA synthesis, whereas the ***A2*** selective antagonist 3,7-dimethyl-1-propargylxanthine (DMPX) decreased adenosine-induced DNA synthesis. Similar effects were observed in another nontumorigenic mouse mammary epithelial line, HC11,. . . nontumorigenic human lines MCF-10A and 184.A1. Binding studies indicated that NMuMG cells contained approximately 3200 A1 receptors and about 5300 ***A2*** receptors per cell. Both CGS-21680 and CHA increased GTPase activity in isolated cell membranes, whereas only CGS-21680 increased activity of. . . be a possible growth promoting agent in mammary tissue, and this effect may be mediated by extracellular receptors of the ***A2*** type.

=> d l8 kwic 11-20

L8 ANSWER 11 OF 108 MEDLINE on STN
SO BRITISH JOURNAL OF PHARMACOLOGY, ***(1998 Jul)*** 124 (5) 964-70.
Journal code: 7502536. ISSN: 0007-1188.
AB . . . prostatic half of the vas deferens the A1 selective adenosine receptor agonists, N6-cyclopentyladenosine (CPA) and (2S)-N6-[2-endo-norbornyl]adenosine ((S)-ENBA) and the non-selective A1/ ***A2*** ***adenosine*** ***receptor*** ***agonist*** , 5'-N-ethylcarboxamidoadenosine (NECA) inhibited electrically-evoked contractions (pIC50+/-s.e.mean values 6.15+/-0.24, 5.99+/-0.26 and 5.51+/-0.24, respectively). The responses to CPA were blocked by the. . . predominant in the prostatic half of the vas deferens). At the epididymis, where electrically-evoked contractions are entirely adrenergic, the predominant ***adenosine*** ***receptor*** ***agonist*** effect is a potentiation of alpha1-adrenoceptor-, but not of ATP-induced contractility.

L8 ANSWER 12 OF 108 MEDLINE on STN
TI Characterization of biochemical effects of CGS 21680C, an ***A2*** - ***adenosine*** ***receptor*** ***agonist*** , in the mammalian ventricle.
SO JOURNAL OF CARDIOVASCULAR PHARMACOLOGY, ***(1997 Dec)*** 30 (6) 750-8.
Journal code: 7902492. ISSN: 0160-2446.
AB Effects of a putative ***A2*** - ***adenosine*** ***receptor*** ***agonist*** 2-[(p-2-carboxyethyl)-phenethylamino]-5'-N-ethyl-carboxamide-adeno sine (CGS 21680C) on force of contraction, protein phosphorylation, cyclic adenosine monophosphate (cAMP) content, and the

0.2 to 13.0 +/- 0.6 pmol/mg protein, and this effect was completely abolished by ***A2*** -adenosine receptor antagonist 9-chloro-2-(2-furanyl)-5,6-dihydro-1,2,4-triazolo-(1,5-c)quinazolin++ +-5-imine (CGS 15943A). CGS 21680C (10 microM) inhibited PDE isoenzymes I, II, III, IV by 7.0, 8.3,. . .

L8 ANSWER 13 OF 108 MEDLINE on STN
SO EUROPEAN JOURNAL OF PHARMACOLOGY, ***(1997 Oct 29)*** 338 (1) 11-6.
Journal code: 1254354. ISSN: 0014-2999.
AB . . . effect produced by morphine. However, the morphine response was decreased and increased by the lower and higher doses of the ***adenosine*** ***receptor*** ***agonist*** , CHA (N6-cyclohexyladenosine), respectively. The adenosine receptor antagonist, theophylline, decreased, but 8-phenyltheophylline increased, the response induced by morphine. Naloxone inhibited the. . . catalepsy induced by morphine or morphine + NECA but not that induced by NECA alone. It is concluded that adenosine ***A2*** receptor activation increases, while adenosine A1 receptor stimulation decreases, the morphine cataleptogenic response. The response to morphine may be mediated. . .

L8 ANSWER 14 OF 108 MEDLINE on STN
SO CIRCULATION, ***(1997 Nov 4)*** 96 (9 Suppl) II-227-32.
Journal code: 0147763. ISSN: 0009-7322.
AB BACKGROUND: Previous experiments have shown that infusion of either adenosine (ADO) or an ***adenosine*** ***receptor*** ***agonist*** during reperfusion after hypothermic ischemia improved the recovery of ventricular function in neonatal lamb hearts. Adenosine has multiple actions that might be beneficial during postischemic reperfusion, and the ***A2*** effects include both coronary vasodilator and leukocyte inhibitory effects. In the current experiment we investigated the relationship between the coronary blood flow (CBF) effects of ***A2*** stimulation and the recovery of postischemic ventricular function. METHODS AND RESULTS: Two hours of 10 degrees C cardioplegic ischemia was. . . reperfusion, Group II received 350 micromol/L ADO, Group III received ADO and 100 nmol/L DPCPX (A1 antagonist) to achieve an ***A2*** effect, Group IV received 0.25 micromol/L CPCA (***A2*** agonist), and Group V received ADO and DPCPX but CBF was limited to that of Group I levels. At 30. . . and IV was CBF higher than in Group I (G-1=116+/-54%, G-II=116+/-27%, G-III=210+/-67%, G-IV=239+/-85%, G-V=130+/-8%, P<.05). CONCLUSIONS: Reperfusion under conditions of ***A2*** stimulation by ADO, by an ***A2*** agonist, or by ADO plus A1 blockade was associated with improved recovery of LV function. The early ***A2*** effect seems to be related to coronary vasodilation because reduced CBF (equal to Group I) in Group V reduced early. . . higher DP and dP/dt. These findings suggest that mechanisms in addition to vasodilation are involved in the beneficial effects of ***A2*** stimulation during postischemic reperfusion.

L8 ANSWER 15 OF 108 MEDLINE on STN
TI Wound healing is accelerated by agonists of adenosine ***A2*** (G alpha s-linked) receptors.
SO JOURNAL OF EXPERIMENTAL MEDICINE, ***(1997 Nov 3)*** 186 (9) 1615-20.
Journal code: 2985109R. ISSN: 0022-1007.
AB . . . mice was significantly accelerated by topical application of the specific A2A receptor agonist CGS-21680 (50% closure by day 2 in ***A2*** receptor antagonists. In rats rendered diabetic (streptozotocin-induced diabetes mellitus) wound healing was impaired as compared to nondiabetic rats; CGS-21680 significantly. . . observed in untreated normal rats. These results appear to constitute the first evidence that a small molecule, such as an ***adenosine*** ***receptor*** ***agonist*** , accelerates wound healing in both normal animals and in animals with impaired wound healing.

L8 ANSWER 16 OF 108 MEDLINE on STN
SO ACTA PHYSIOLOGICA HUNGARICA, ***(1996)*** 84 (3) 339-41.
Journal code: 8309201. ISSN: 0231-424X.
AB In isolated guinea pig pulmonary arteries (precontracted with 1 microM noradrenaline) N6-cyclopentyladenosine (CPA), a selective A1 ***adenosine*** ***receptor*** ***agonist*** , exerted a concentration-dependent contraction, whereas 5'-N-ethylcarboxamidoadenosine (NECA), a non-selective A1/ ***A2*** receptor agonist, in the presence of DPCPX (a highly selective A1 receptor antagonist), produced a concentration-related rapid relaxation. Pulmonary arteries. . .

SO CELLULAR AND MOLECULAR BIOLOGY, ***(1997 May)*** 43 (3) 345-9.
Journal code: 9216789. ISSN: 0145-5680.
AB . . . Murine J774.1 macrophage cells were found to predominantly express adenosine A3 receptor RNA relative to adenosine A1 receptor or adenosine ***A2*** receptor RNA. Adenosine receptor agonists, in a dose-dependent manner characteristic of the adenosine A3 receptor, blocked endotoxin-induction of the TNF-alpha. . . . gene and TNF-alpha protein expression in the J774.1 macrophage cell line. The adenosine A3 receptor antagonist BW-1433 dose-dependently reversed this ***adenosine*** ***receptor*** ***agonist*** inhibitory effect on TNF-alpha gene expression. Thus, the binding of adenosine receptor agonists to the adenosine A3 receptor interrupts the. . .

L8 ANSWER 18 OF 108 MEDLINE on STN
SO EXPERIMENTAL CELL RESEARCH, ***(1997 May 25)*** 233 (1) 187-97.
Journal code: 0373226. ISSN: 0014-4827.
AB The effect of 2-chloroadenosine (2CA), an ***adenosine*** ***receptor*** ***agonist*** , on the activation status of mouse natural killer (NK) cells was determined. Splenic lymphocytes incubated with 2CA exocytosed an NK. . . . the nucleoside uptake blockers NBTI, dilazep, or dipyridamole, indicating the involvement of an extracellular receptor. However, adenosine or other A1, ***A2*** , or A3 cell-surface adenosine receptor agonists failed to trigger the exocytotic process. Furthermore, the nonselective adenosine receptor antagonist theophylline, as well as the selective A1 receptor antagonist DPCPX and the selective ***A2*** receptor antagonist DMPX, did not interfere with 2CA-induced BLT esterase secretion. These data suggest that 2CA acts on NK cells via a novel (non-A1/ ***A2*** /A3) cell-surface receptor. Genistein, a protein tyrosine kinase inhibitor, and calphostin C, a protein kinase C inhibitor, both interfered with 2CA-induced. . .

L8 ANSWER 19 OF 108 MEDLINE on STN
SO BRAIN RESEARCH, ***(1996 Nov 18)*** 740 (1-2) 329-36.
Journal code: 0045503. ISSN: 0006-8993.
AB . . . accepted to act as an inhibitory neuromodulator in the mammalian central nervous system. In the present study, we examined whether ***adenosine*** ***receptor*** ***agonist*** modifies the photic entraining responses in the rat suprachiasmatic nucleus both in vivo and in vitro. Light (200 lux, 15 min)-induced phase shifts of hamster wheel-running rhythms was attenuated by a systemic administration of A1- ***adenosine*** ***receptor*** ***agonist*** N6-cyclohexyladenosine (N-CHA) in a dose-dependent manner; 0.5 mg/kg N-CHA caused 60% inhibition of light-induced phase shifts. On the other hand, ***A2*** - ***adenosine*** ***receptor*** ***agonist*** N6-[2-(3,5-dimethoxyphenyl)-2-(2-methylphenyl)-ethyl]adenosine (DPMA) failed to inhibit light-induced phase shifts. Systemic administration of N-CHA but not of DPMA inhibited light (300 lux,. . .

L8 ANSWER 20 OF 108 MEDLINE on STN
SO NEUROSCIENCE LETTERS, ***(1996 Nov 1)*** 218 (2) 91-4.
Journal code: 7600130. ISSN: 0304-3940.
AB . . . cells using the enzyme-linked immunosorbent assay (ELISA) for determining DNA fragmentation. Twelve hours exposure to micromolar levels of the unselective ***adenosine*** ***receptor*** ***agonist*** 2-chloro-adenosine led to the appearance of DNA fragments in the cytosolic fraction preceding damage of the plasma membrane. This effect was still seen in the presence of an adenosine uptake blocker. Conventional A1, ***A2*** or A3 agonists and antagonists were rather ineffective, suggesting mediation via an atypical adenosine receptor subtype. Microglial DNA fragmentation was. . .

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E3            0 --> DE ZWART/AU
E4            5     DE ZWART A/AU
E5            5     DE ZWART A J/AU
E6            1     DE ZWART ANNEMIEKE/AU
E7            9     DE ZWART B C/AU
E8           15     DE ZWART B C H/AU
E9            1     DE ZWART BART C/AU
E10           4     DE ZWART BART C H/AU
E11          56     DE ZWART D/AU
E12           7     DE ZWART D F/AU

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E1            4     DE ZWART W/AU
E2           12     DE ZWART W M/AU
E3            0 --> DE ZWART, M/AU
E4            1     DE ZWARTE D/AU
E5            3     DE ZWARTE PIETER JOHANNES GERRIT/AU
E6            1     DE ZWEERS G A/AU
E7            2     DE ZWIREK C S/AU
E8            2     DE ZYLVA E R A/AU
E9            2     DE ZYLVA G/AU
E10           1     DE ZYLVA M N/AU
E11           2     DE ZYLVA T S U/AU
E12           1     DE ZYLVA W H/AU

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E1            4     DE ZWART W/AU
E2           12     DE ZWART W M/AU
E3            0 --> DE ZWART, M?/AU
E4            1     DE ZWARTE D/AU
E5            3     DE ZWARTE PIETER JOHANNES GERRIT/AU
E6            1     DE ZWEERS G A/AU
E7            2     DE ZWIREK C S/AU
E8            2     DE ZYLVA E R A/AU
E9            2     DE ZYLVA G/AU
E10           1     DE ZYLVA M N/AU
E11           2     DE ZYLVA T S U/AU
E12           1     DE ZYLVA W H/AU

=> s e1-2
L9           16 ("DE ZWART W"/AU OR "DE ZWART W M"/AU)

=> dup rem l9
PROCESSING COMPLETED FOR L9
L10          12 DUP REM L9 (4 DUPLICATES REMOVED)
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L10 ANSWER 1 OF 12 MEDLINE on STN
ACCESSION NUMBER: 2001316254 MEDLINE
DOCUMENT NUMBER: 21282678 PubMed ID: 11388979
TITLE: Cannabis regimes.
COMMENT: Comment on: Br J Psychiatry. 2001 Feb;178:123-8
Comment in: Br J Psychiatry. 2001 Oct;179:369-70
AUTHOR: ***de Zwart W*** ; van Laar M
SOURCE: BRITISH JOURNAL OF PSYCHIATRY, (2001 Jun) 178 574-5.
Journal code: 0342367. ISSN: 0007-1250.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Commentary
Letter
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010702
Last Updated on STN: 20030124
Entered Medline: 20010628

L10 ANSWER 2 OF 12 EMBASE
on STN
ACCESSION NUMBER: 2001210859 EMBASE
TITLE: Cannabis regimes [3].
AUTHOR: ***De Zwart W.*** ; Van Laar M.
CORPORATE SOURCE: W. De Zwart, Trimbos-Institute, NLD Inst. Mental Hlth./Addiction, PO 725, 3500 AS Utrecht, Netherlands
SOURCE: British Journal of Psychiatry, (2001) 178/JUNE (574-575).
Refs: 6
ISSN: 0007-1250 CODEN: BJPYAJ
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Letter
FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology
032 Psychiatry
040 Drug Dependence, Alcohol Abuse and Alcoholism
LANGUAGE: English

L10 ANSWER 3 OF 12 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 1999458895 MEDLINE
DOCUMENT NUMBER: 99458895 PubMed ID: 10527530
TITLE: The effectiveness of policy and health education strategies for reducing adolescent smoking: a review of the evidence.
AUTHOR: Willemsen M C; ***De Zwart W M***
CORPORATE SOURCE: Dutch Foundation on Smoking and Health, The Hague, The Netherlands.. mwillemsen@stivoro.nl
SOURCE: JOURNAL OF ADOLESCENCE, (1999 Oct) 22 (5) 587-99.
Journal code: 7808986. ISSN: 0140-1971.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991118
AB This paper identifies the most effective measures to prevent smoking among adolescents. A review was made of the international literature concerning a ban on tobacco advertising, restrictions on sales to youth, product regulation, price increase of cigarettes and educational strategies. It is concluded that isolated measures produce little effect. Most effect may be expected from a combination of a complete ban on tobacco advertising, increasing prices, restricting tobacco product sales to tobacconists, mass media education aimed at youth and intensifying school education. A less effective measure is limiting the age at which adolescents are allowed to buy cigarettes.

L10 ANSWER 4 OF 12 EMBASE
on STN
ACCESSION NUMBER: 1999377864 EMBASE
TITLE: Trends and patterns in illicit drug use among students aged 12 to 18 in the Netherlands.
AUTHOR: Kuipers S.B.M.; ***De Zwart W.M.***
CORPORATE SOURCE: W.M. De Zwart, Trimbos Institute, P.O. Box 725, 3500 AS Utrecht, Netherlands

Refs: 34
ISSN: 0022-0426 CODEN: JDGIA6
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology
040 Drug Dependence, Alcohol Abuse and Alcoholism
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The tradition of conducting surveys to measure substance use among youngsters in the Netherlands dates back to 1969. Since that time, a number of prevalence surveys have been conducted regarding illicit drug use, particularly the use of cannabis. Comparing these survey results has been problematic, however, due to differences in sampling approaches and data collection methods. This article provides a description and analysis of the early student drug use studies, concentrating on their contributions to our knowledge about changing patterns of use among these groups. It also details the more problematic aspects of this data, difficulties associated with the manner in which the studies were conducted. Recent efforts have been attempted to correct these difficulties by standardizing methodological approaches. The Peilstations-Survey, a national evaluation of school students 12-18 years of age, has been conducted four times since 1984. Results indicate an increase in both the lifetime and last-month prevalence of cannabis use over the 1984-1996 period, although only a minority of the students reported using cannabis on a regular basis. The general characteristics of very regular cannabis users have changed somewhat over time, overall becoming more like those of current non-users. Peer influence, in particular, has remained an important predictor of cannabis-using behavior.

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ACCESSION NUMBER: 1998368842 EMBASE
TITLE: [Substance use in secondary specialized education and truant care projects in 1997].
MIDDELENGEBRUIK IN HET VOORTGEZET SPECIAAL ONDERWIJS EN SPIJBELOPVANGPROJECTEN IN 1997.
AUTHOR: Stam H.; Mensink C.; ***De Zwart W.M.***
CORPORATE SOURCE: H. Stam, Trimbos-Instituut, Postbus 725, 3500 AS Utrecht, Netherlands
SOURCE: Tijdschrift voor Alcohol, Drugs en Andere Psychotrope Stoffen, (1998) 23/1-2 (17-23).
ISSN: 0378-2778 CODEN: TADSDB
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology
040 Drug Dependence, Alcohol Abuse and Alcoholism
LANGUAGE: Dutch

L10 ANSWER 6 OF 12 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 97317215 EMBASE
DOCUMENT NUMBER: 1997317215
TITLE: [Substance abuse among young students has increased].
MIDDELENGEBRUIK ONDER SCHOLIEREN TOEGENOMEN.
AUTHOR: ***De Zwart W.M.*** ; Stam H.; Kuipers S.B.M.
CORPORATE SOURCE: W.M. De Zwart, Trimbos-Instituut, Postbus 725, 3500 AS Utrecht, Netherlands
SOURCE: Tijdschrift voor Alcohol, Drugs en Andere Psychotrope Stoffen, (1997) 22/2 (74-79).
ISSN: 0378-2778 CODEN: TADSDB
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology
040 Drug Dependence, Alcohol Abuse and Alcoholism
LANGUAGE: Dutch

L10 ANSWER 7 OF 12 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 94300484 MEDLINE
DOCUMENT NUMBER: 94300484 PubMed ID: 7913127
TITLE: Research methods for illegal drug use in hidden populations: summary report of a European invited expert meeting.
AUTHOR: van de Goor L A; Garretsen H F; Kaplan C; Korf D; Spruit I P; ***de Zwart W M***
CORPORATE SOURCE: European Addiction Research Institute-Erasmus University,

SOURCE: JOURNAL OF PSYCHOACTIVE DRUGS, (1994 Jan-Mar) 26 (1) 33-40.
Journal code: 8113536. ISSN: 0279-1072.
PUB. COUNTRY: United States
DOCUMENT TYPE: Conference; Conference Article; (CONGRESSES)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199408
ENTRY DATE: Entered STN: 19940818
Last Updated on STN: 19990129
Entered Medline: 19940809

AB An Invited European Expert Group Meeting was held in Rotterdam that focused on research methods for hidden populations using illicit drugs. Experts from most European Community member states participated and contributed state-of-the-art presentations on various research methodologies. Attention was paid to the more quantitatively oriented research methods, such as surveys using questionnaires, interviews, and routine statistics from treatment and criminal justice as well as to more ethnographically oriented research methodologies. Recommendations were formulated for the near future: research methodology needs to meet all the classical methodological criteria, such as clear definitions, tests on reliability and validity, and clear sampling procedures. Interfacing methods is the key phrase. More quantitatively oriented methods, such as interviewing a random sample from a household survey, seem unsuitable for research on illicit drugs, except perhaps for the use of cannabis. A multifactorial problem, such as illicit drug use and related problems, should be approached in a multidisciplinary way; that is, the integration of different research methodologies. Comparability between individual research projects in different countries requires not only technical adjustments of the data, but also a "framework for communication." Data always need to be interpreted in terms of cultural context. A similar framework should enhance studies with respect to comparison of drug policies and their consequences in different cities or countries.

L10 ANSWER 8 OF 12 EMBASE
on STN
ACCESSION NUMBER: 93117761 EMBASE
DOCUMENT NUMBER: 1993117761
TITLE: [Invited Expert Meeting on Illegal Drug Use: Research methods for hidden populations, Rotterdam, 28-30 October 1992].
INVITED EXPERT MEETING ON ILLEGAL DRUG USE: RESEARCH METHODS FOR HIDDEN POPULATIONS, ROTTERDAM, 23-30 OKTOBER 1992.
AUTHOR: ***De Zwart W.M.*** ; Van De Goor L.A.M.
CORPORATE SOURCE: Nederlands Inst. voor Alcohol/Drugs,Utrecht, Netherlands
SOURCE: Tijdschrift voor Alcohol, Drugs en Andere Psychotrope Stoffen, (1992) 18/2 (110-113).
ISSN: 0378-2778 CODEN: TADSDB
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 040 Drug Dependence, Alcohol Abuse and Alcoholism
LANGUAGE: Dutch

L10 ANSWER 9 OF 12 EMBASE
on STN DUPLICATE 3
ACCESSION NUMBER: 91235976 EMBASE
DOCUMENT NUMBER: 1991235976
TITLE: Treatment of women alcoholics, clinical and epidemiological data.
AUTHOR: ***De Zwart W.***
CORPORATE SOURCE: Nederlands Instituut voor Alcohol en Drugs (NIAD), Utrecht, Netherlands
SOURCE: Alcoholism, (1991) 27/1-2 (17-31).
ISSN: 0002-502X CODEN: ALCMAN
COUNTRY: Yugoslavia
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 032 Psychiatry
040 Drug Dependence, Alcohol Abuse and Alcoholism
LANGUAGE: English

L10 ANSWER 10 OF 12 EMBASE
on STN
ACCESSION NUMBER: 90057640 EMBASE
DOCUMENT NUMBER: 1990057640
TITLE: [Treatment of female alcoholics, clinical and epidemiological data].

EPIDEMIOLOGISCHE GEGEVENS.
UTHOR: ***De Zwart W.M.***
OURCE: Tijdschrift voor Alcohol, Drugs en Andere Psychotrope Stoffen, (1989) 15/4 (138-145).
ISSN: 0378-2778 CODEN: TADSDB
OUNTRY: Netherlands
OCUMENT TYPE: Journal; Article
ILE SEGMENT: 032 Psychiatry
040 Drug Dependence, Alcohol Abuse and Alcoholism
ANGUAGE: Dutch
UMMARY LANGUAGE: English
B In the first part of this paper epidemiological data on female problem drinking were presented. Conclusions were that the percentage of women with alcohol problems has increased during the seventies but stabilized in the eighties. One out of every five problem drinkers is a woman. This conclusion was based on admission data of health care agencies. In the Netherlands female problem drinkers get little attention from researchers. It is often difficult to include an adequate number of women in a research sample, so it regularly happens that researchers ignore women in their projects. The second part of the paper concentrates on data from research in an all women's alcohol clinic. Women in the age of 35-45 were overrepresented among the clients, as were the divorced and widowed women. A remarkable result was the finding that 30% of the women who came for intake did not actually enter treatment. The length of the waitinglist was an important explanatory factor. Another result was that the problems women wanted to be treated in the clinic differed from the problems reported by the counselors who referred them. Counselors advised to focus in treatment on human relations problems and identity problems. The women themselves, however, reported frequently feelings of inferiority and feelings of guilt. The results at follow-up, 4.5 months after discharge from the clinic, were rather positive. 23% had been abstinent, 32% did drink alcohol but not in the previous month, while 27% used alcohol the last month before answering the questionnaire. However, the non-response group remained in treatment for a shorter period and more frequently left the programme against staff advice. Both these factors have been associated with poorer treatment effects. So the results of this part of the study may not represent all women well enough.

10 ANSWER 11 OF 12 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
CCESSION NUMBER: 86103171 EMBASE
OCUMENT NUMBER: 1986103171
ITLE: Local authorities and drug policy.
UTHOR: ***De Zwart W.M.***
ORPORATE SOURCE: Netherlands
OURCE: Tijdschrift voor Alcohol, Drugs en Andere Psychotrope Stoffen, (1986) 12/1 (22-24).
CODEN: TADSDB
OUNTRY: Netherlands
OCUMENT TYPE: Journal
ILE SEGMENT: 036 Health Policy, Economics and Management
040 Drug Dependence, Alcohol Abuse and Alcoholism
ANGUAGE: Dutch
B The article presents a summary of the main papers given during the Dutch Congress on Local Authorities and Drug Policy, organised by the Council of European Communities, the The Hague local Authority and the Zeestraat Addiction Center. During the congress speakers form several local and regional authorities (Berlin, Amsterdam, Singapore, Newark, London) presented treatment and prevention models operated in their district and an outline of the narcotic crimes policy operated by their local police forces.

10 ANSWER 12 OF 12 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
CCESSION NUMBER: 85054966 EMBASE
OCUMENT NUMBER: 1985054966
ITLE: Addiction on prescription?.
UTHOR: ***De Zwart W.M.***
ORPORATE SOURCE: Netherlands
OURCE: Tijdschrift voor Alcohol, Drugs en Andere Psychotrope Stoffen, (1984) 10/4 (173-178).
CODEN: TADSDB
OUNTRY: Netherlands
OCUMENT TYPE: Journal
ILE SEGMENT: 040 Drug Dependence, Alcohol Abuse and Alcoholism
ANGUAGE: Dutch

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=> e dezwart, m?/ au
E1            4     DEZWART F H W/AU
E2            1     DEZWART S T/AU
E3            0 --> DEZWART, M?/AU
E4            1     DEZWARTE H L/AU
E5            4     DEZYNA M/AU
E6            4     DEZZ ROPP J/AU
E7            1     DEZZA/AU
E8           10     DEZZA A/AU
E9            1     DEZZA FILIPPO/AU
E10           3     DEZZA G/AU
E11           2     DEZZA G C/AU
E12          82     DEZZA L/AU

=> s retinal endothelial cells
L11         759 RETINAL ENDOTHELIAL CELLS

=> s l11 and py<2000
   4 FILES SEARCHED...
L12         385 L11 AND PY<2000

=> s l12 and culture
L13         132 L12 AND CULTURE

=> s l12 (p)culture
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L24 (P)CULTURE'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L25 (P)CULTURE'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L26 (P)CULTURE'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L27 (P)CULTURE'
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FIELD CODE - 'AND' OPERATOR ASSUMED 'L28 (P)CULTURE'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L29 (P)CULTURE'
L14         132 L12 (P) CULTURE

=> d l14 ibib abs 1-10

L14  ANSWER 1 OF 132     MEDLINE on STN
ACCESSION NUMBER:    2003455203     MEDLINE
DOCUMENT NUMBER:     22878697   PubMed ID: 14517453
TITLE:               The formation of tubular structures by endothelial cells is
                     under the control of fibrinolysis and mechanical factors.
AUTHOR:              Vailhe B; Lecomte M; Wiernsperger N; Tranqui L
CORPORATE SOURCE:    Laboratoire de Bioenergetique Fondamentale et Appliquee,
                     Universite Joseph Fourier, B.P.53X, 38041 Grenoble Cedex 9,
                     France.
SOURCE:              Angiogenesis,   ***(1998)***   2 (4) 331-44.
                     Journal code: 9814575. ISSN: 0969-6970.
PUB. COUNTRY:        Netherlands
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
ENTRY MONTH:         200310
ENTRY DATE:          Entered STN: 20031001
                     Last Updated on STN: 20031010
                     Entered Medline: 20031009
AB   This study highlights the importance of several factors involved in the
     formation of capillary-like structure formation (CLS) using Human
     Umbilical Vein Endothelial Cells (HUVEC) and Bovine   ***Retinal***
       ***Endothelial***     ***Cells***   (BREC) cultured on fibrin gels.  The
     fibrin concentration inducing (CLS) was 0.5 mg/ml for HUVEC and 8 mg/ml
     for BREC.  The high fibrin concentration required for the latter cells
     appeared necessary to counterbalance the extensive fibrinolysis of the gel
     by the BREC.  Fibrin degradation products measured in the   ***culture***
     media showed that fibrin degradation was mandatory but not sufficient for
     CLS formation.  Fibrin degradation acted in concert with the mechanical,
     concentration dependent properties of the gels to induce CLS.  For
     example, HUVEC did not form CLS on a rigid fibrin of 8 mg/ml in spite of
     fibrinolysis.  As cell reorganisation occurred, the fibrin was disrupted
     (HUVEC) or pleated (BREC) giving indirect proof of the development of
     mechanical forces.  During CLS formation, an increasing amount of latent
     TGFbeta1 was measured in the medium (1000-1700 pg/ml).  The active form of
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antibody to the medium did not influence the formation of the CLS network. Yet, added activated TGF-beta1 led to the formation of less organised structures, that were completely abolished by the concomitant addition of the same anti-TGF-beta1 antibody. Thus, it is likely that TGF-beta1 secreted by the endothelial cells remained in its latent form. In conclusion, a balance between the mechanical properties of fibrin and the fibrinolytic activity of each cell type may regulate CLS formation in our models. We think that the high fibrinolitic activity of the BREC may represent a defense mechanism to protect the retina against thrombosis-induced damage in vivo.

L14 ANSWER 2 OF 132 MEDLINE on STN
ACCESSION NUMBER: 2000488645 MEDLINE
DOCUMENT NUMBER: 20492729 PubMed ID: 11039605
TITLE: VEGF-dependent signaling in retinal microvascular endothelial cells.
AUTHOR: Enaida H; Kabuyama Y; Oshima Y; Sakamoto T; Kato K; Kochi H; Homma Y
CORPORATE SOURCE: Department of Biomolecular Science, Fukushima Medical University School of Medicine, Fukushima City, Japan.
SOURCE: FUKUSHIMA JOURNAL OF MEDICAL SCIENCE, ***(1999 Dec)*** 45 (2) 77-91.
Journal code: 0374626. ISSN: 0016-2590.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001117
AB We examined the effect of vascular endothelial growth factor (VEGF) on intracellular signal transduction pathways using isolated bovine microvascular endothelial cells (BREC). When cell growth was determined by [3H]thymidine incorporation, it was significantly stimulated by VEGF stimulation. In situ hybridization results also demonstrated that c-fos expression was enhanced by the stimulation. Although BREC expressed Flt-1 and Flk-1 as VEGF receptors at similar levels, VEGF stimulation preferentially enhanced the activity of Flt-1 tyrosine kinase. This stimulation initiated an increase in the level of GTP-form Ras and the activation of mitogen activated protein kinase (MAPK). On the other hand, BREC expressed the Janus kinase (Jak) family members Jak1, Jak2, and Tyk2, and the signal transducers and activators of transcription (Stat) family members Stat1, Stat3, and Stat6. These molecules were tyrosine phosphorylated under ***culture*** conditions used, and the phosphorylation of Tyk2 and Stat6 was specifically enhanced by VEGF stimulation. These results demonstrate that, in addition to Ras/MAPK pathways, the Flt-1/Tyk2/Stat6 pathway is important in VEGF signaling in BREC. These signal transduction systems may regulate the growth of ***retinal*** ***endothelial*** ***cells*** .

L14 ANSWER 3 OF 132 MEDLINE on STN
ACCESSION NUMBER: 1999451092 MEDLINE
DOCUMENT NUMBER: 99451092 PubMed ID: 10521243
TITLE: Adenosine receptor activation induces vascular endothelial growth factor in human ***retinal*** ***endothelial*** ***cells*** .
AUTHOR: Grant M B; Tarnuzzer R W; Caballero S; Ozeck M J; Davis M I; Spoerri P E; Feoktistov I; Biaggioni I; Shryock J C; Belardinelli L
CORPORATE SOURCE: Department of Medicine, Ophthalmology and Pharmacology, University of Florida, Gainesville, Fla 32610-0226, USA.. grantma@medicine.ufl.edu
SOURCE: CIRCULATION RESEARCH, ***(1999 Oct 15)*** 85 (8) 699-706.
Journal code: 0047103. ISSN: 1524-4571.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20010521
Entered Medline: 19991104
AB Adenosine, released in increased amounts by hypoxic tissues, is thought to be an angiogenic factor that links altered cellular metabolism caused by

4 subtypes of G protein-coupled receptors, termed A(1), A(2A), A(2B), and A(3). We investigated whether adenosine causes proliferation of human ***retinal*** ***endothelial*** ***cells*** (HRECs) and synthesis of vascular endothelial growth factor (VEGF) and, if so, which adenosine receptor subtype mediates these effects. The nonselective adenosine receptor agonist 5'-N-ethylcarboxamidoadenosine (NECA), in a concentration-dependent manner, increased both VEGF mRNA and protein expression by HRECs, as well as proliferation. This proliferative effect of NECA was inhibited by the addition of anti-human VEGF antibody. NECA also increased insulin-like growth factor-I and basic fibroblast growth factor mRNA expression in a time-dependent manner and cAMP accumulation in these cells. In contrast, neither the A(1) agonist N(6)-cyclopentyladenosine nor the A(2A) agonist 2-p-(2-carboxyethyl) phenethylamino-NECA caused any of the above effects of NECA. The effects of NECA were not significantly attenuated by either the A(2A) antagonist SCH58261 or the A(1) antagonist 8-cyclopentyl-1, 3-dipropylxanthine. However, the nonselective adenosine receptor antagonist xanthine amine congener completely inhibited the effects of NECA. Addition of antisense oligonucleotide complementary to A(2B) adenosine receptor mRNA inhibited VEGF protein production by HRECs after NECA stimulation. Thus, the A(2B) adenosine receptor subtype appears to mediate the actions of adenosine to increase growth factor production, cAMP content, and cell proliferation of HRECs. Adenosine activates the A(2B) adenosine receptor in HRECs, which may lead to neovascularization by a mechanism involving increased angiogenic growth factor expression.

L14 ANSWER 4 OF 132 MEDLINE on STN
ACCESSION NUMBER: 1999394621 MEDLINE
DOCUMENT NUMBER: 99394621 PubMed ID: 10466745
TITLE: Endothelial cell chemotaxic activity expressed in rat placenta is not associated with prolactin-like proteins B and C.
AUTHOR: Charles G D; Grant M B; Medrano T A; Saunders P; Edery M; Kelly P A; Shiverick K T
CORPORATE SOURCE: Department of Pharmacology & Therapeutics, University of Florida, Gainesville 32610-0267, USA.
CONTRACT NUMBER: EY07739 (NEI)
SOURCE: LIFE SCIENCES, ***(1999)*** 65 (8) 795-804.
Journal code: 0375521. ISSN: 0024-3205.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 19990925
Last Updated on STN: 19990925
Entered Medline: 19990914
AB Conditioned medium from gestation day 18 rat placental cultures showed potent stimulation of the directional migration of human ***retinal*** ***endothelial*** ***cells*** . To examine the role of major secreted placental proteins in this chemotaxic activity, prolactin-like proteins (PLPs)-B and C were purified from rat placenta using immuno-affinity chromatography. In contrast to conditioned medium, native PLP-B and PLP-C preparations failed to show any significant stimulation of endothelial cell migration. This study further examined the ability of PLP-B to bind to rat receptors for growth hormone (GH-R) and prolactin (PRL-R). In competitive binding assays with [125I]-hGH, neither native nor recombinant PLP-B preparations showed significant high affinity binding to the transfected rat GH-R or PRL-R. In summary, neither PLP-B nor PLP-C exhibit the potent chemotaxis stimulatory activity of placental conditioned media, nor does PLP-B show evidence of ability to act via rat GH or PRL receptors.

L14 ANSWER 5 OF 132 MEDLINE on STN
ACCESSION NUMBER: 1999367479 MEDLINE
DOCUMENT NUMBER: 99367479 PubMed ID: 10438525
TITLE: Vascular endothelial growth factor induces rapid phosphorylation of tight junction proteins occludin and zonula occluden 1. A potential mechanism for vascular permeability in diabetic retinopathy and tumors.
AUTHOR: Antonetti D A; Barber A J; Hollinger L A; Wolpert E B; Gardner T W
CORPORATE SOURCE: Penn State Retina Research Group, Pennsylvania State University College of Medicine, Hershey, Pennsylvania 17033, USA.. dantonetti@psu.edu
CONTRACT NUMBER: RO1 EY/DK12021 (NEI)

274 (33) 23463-7.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 19990913
Last Updated on STN: 19990913
Entered Medline: 19990901

AB Vascular endothelial growth factor (VEGF) may have a physiologic role in regulating vessel permeability and contributes to the pathophysiology of diabetic retinopathy as well as tumor development. We set out to ascertain the mechanism by which VEGF regulates paracellular permeability in rats. Intra-ocular injection of VEGF caused a post-translational modification of occludin as determined by a gel shift from 60 to 62 kDa. This event began by 15 min post-injection and was maximal by 45 min. Alkaline phosphatase treatment revealed this modification was caused by a change in occludin phosphorylation. In addition, the quantity of extracted occludin increased 2-fold in the same time frame. The phosphorylation and increased extraction of occludin was recapitulated in ***retinal*** ***endothelial*** ***cells*** in ***culture*** after VEGF stimulation. The data presented herein are the first demonstration of a change in the phosphorylation of this transmembrane protein under conditions of increased endothelial permeability. In addition, intra-ocular injection of VEGF also caused tyrosine phosphorylation of ZO-1 as early as 15 min and increased phosphorylation 4-fold after 90 min. In conclusion, VEGF rapidly increases occludin phosphorylation as well as the tyrosine phosphorylation of ZO-1. Phosphorylation of occludin and ZO-1 likely contribute to regulated endothelial paracellular permeability.

L14 ANSWER 6 OF 132 MEDLINE on STN
ACCESSION NUMBER: 1999260263 MEDLINE
DOCUMENT NUMBER: 99260263 PubMed ID: 10331420
TITLE: Vascular endothelial growth factor activates nuclear factor-kappaB and induces monocyte chemoattractant protein-1 in bovine ***retinal*** ***endothelial*** ***cells*** .
AUTHOR: Marumo T; Schini-Kerth V B; Busse R
CORPORATE SOURCE: Institut fur Kardiovaskulare Physiologie, Klinikum der Johann Wolfgang Goethe Universitat, Frankfurt am Main, Germany.. r.busse@em.uni-frankfurt.de
SOURCE: DIABETES, ***(1999 May)*** 48 (5) 1131-7.
Journal code: 0372763. ISSN: 0012-1797.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990607
Last Updated on STN: 19990607
Entered Medline: 19990527

AB Vascular endothelial growth factor (VEGF) has been suggested to play a role in the pathogenesis of diabetic vascular complications. In the present study, we investigated whether expression of monocyte chemoattractant protein-1 (MCP-1), a chemokine that has been proposed to recruit leukocytes to sites of inflammation, neovascularization, and vascular injury, can be modulated by VEGF in bovine retinal microvascular endothelial cells (BRECs). VEGF induced expression of MCP-1 mRNA in BRECs in a concentration- and time-dependent manner. Secretion of MCP-1 into the ***culture*** medium of BRECs treated with VEGF for 24 h was increased by 2.2-fold compared with the control. Inhibitors of transcription factor NF-kappaB, N-alpha-tosyl-L-lysine chloromethylketone (TLCK) and N-acetylcysteine (NAC), as well as an inhibitor of the extracellular signal-regulated kinase (ERK) pathway, PD 98059, attenuated VEGF-induced expression of MCP-1 mRNA. Using electrophoretic gel mobility shift assay, we observed that VEGF stimulated binding activity of NF-kappaB. VEGF-induced NF-kappaB activation was inhibited by TLCK and NAC, but not by PD 98059. Binding activity of transcription factor AP-1, which is suggested to regulate induction of the MCP-1 gene together with NF-kappaB, was also stimulated by VEGF. PD 98059 inhibited the VEGF-induced activation of AP-1. These results indicate that VEGF induces MCP-1 expression in BRECs most likely by activating NF-kappaB and AP-1 via ERK-independent and -dependent pathways. Activation of NF-kappaB and induction of MCP-1 by VEGF in microvascular endothelial cells may

L14 ANSWER 7 OF 132 MEDLINE on STN
ACCESSION NUMBER: 1999052348 MEDLINE
DOCUMENT NUMBER: 99052348 PubMed ID: 9836530
TITLE: Vascular permeability in experimental diabetes is associated with reduced endothelial occludin content: vascular endothelial growth factor decreases occludin in ***retinal*** ***endothelial*** ***cells*** . Penn State Retina Research Group.
AUTHOR: Antonetti D A; Barber A J; Khin S; Lieth E; Tarbell J M; Gardner T W
CORPORATE SOURCE: Department of Ophthalmology, Penn State Geisinger Health System, Penn State University College of Medicine, Hershey 17033, USA.
CONTRACT NUMBER: K11 EY 00331 (NEI)
SOURCE: DIABETES, ***(1998 Dec)*** 47 (12) 1953-9.
Journal code: 0372763. ISSN: 0012-1797.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981221

AB Blood-retinal barrier (BRB) breakdown is a hallmark of diabetic retinopathy, but the molecular changes that cause this pathology are unclear. Occludin is a transmembrane component of interendothelial tight junctions that may regulate permeability at the BRB. In this study, we examined the effects of vascular endothelial growth factor (VEGF) and diabetes on vascular occludin content and barrier function. Sprague-Dawley rats were made diabetic by intravenous streptozotocin injection, and age-matched animals served as controls. After 3 months, BRB permeability was quantified by intravenous injection of fluorescein isothiocyanate-bovine serum albumin (FITC-BSA), Mr 66 kDa, and 10-kDa rhodamine-dextran (R-D), followed by digital image analysis of retinal sections. Retinal fluorescence intensity for FITC-BSA increased 62% (P < or = 0.05), but R-D fluorescence did not change significantly. Occludin localization at interendothelial junctions was confirmed by immunofluorescence, and relative protein content was determined by immunoblotting of retinal homogenates. Retinal occludin content decreased approximately 35% (P < or = 0.03) in the diabetic versus the control animals, whereas the glucose transporter GLUT1 content was unchanged in rat retinas. Additionally, treatment of bovine ***retinal*** ***endothelial*** ***cells*** in ***culture*** with 0.12 nmol/l or 12 nmol/l VEGF for 6 h reduced occludin content 46 and 54%, respectively. These data show that diabetes selectively reduces retinal occludin protein expression and increases BRB permeability. Our findings suggest that the elevated VEGF in the vitreous of patients with diabetic retinopathy increases vascular permeability by downregulating occludin content. Decreased tight junction protein expression may be an important means by which diabetes causes increased vascular permeability and contributes to macular edema.

L14 ANSWER 8 OF 132 MEDLINE on STN
ACCESSION NUMBER: 1998363137 MEDLINE
DOCUMENT NUMBER: 98363137 PubMed ID: 9699557
TITLE: Glucose-induced increase in paracellular permeability and disruption of beta-receptor signaling in retinal endothelium.
AUTHOR: Haselton F R; Dworska E J; Hoffman L H
CORPORATE SOURCE: Department of Biomedical Engineering, School of Engineering, Vanderbilt University, Nashville, Tennessee 37235, USA.
CONTRACT NUMBER: EY10086 (NEI)
SOURCE: INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE, ***(1998*** *** Aug)*** 39 (9) 1676-84.
Journal code: 7703701. ISSN: 0146-0404.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 19980820
Last Updated on STN: 19980820
Entered Medline: 19980813

endothelial permeability in an in vitro model of the retinal microvasculature. METHODS: The permeability of the endothelial barrier to small solutes was measured in a chromatographic cell column consisting of bovine ***retinal*** ***endothelial*** ***cells*** cultured on porous fibronectin-coated microcarriers. In each cell column, permeability changes were evaluated by comparing the treatment permeability response over time with the initial baseline permeability. Short-term (2-hour) barrier effects of glucose were examined by measuring permeability at 15-minute intervals after an increase in perfusate concentration from baseline (5.5 mM) to high (25 mM) glucose. Long-term (to 57 days) effects were tested by addition of 25 mM glucose to microcarrier cultures. The effect of glucose on beta-receptor signaling was tested by measuring its effect on the permeability decrease produced by 1 microM isoproterenol. RESULTS: An increase from 5.5 mM to 25 mM glucose concentration did not change retinal endothelial cell monolayer permeability (n=6) during 2 hours. However, an increase in monolayer permeability was observed after 19 days (n=8) in the 25-mM glucose ***culture*** . Paralleling this time course, short-term exposure to 25 mM glucose did not prevent a decrease in permeability triggered by the beta-receptor agonist isoproterenol. However, the permeability effect of the agonist was blocked by long-term ***culture*** in 25 mM glucose. Permeability of retinal endothelial monolayers cultured in 5.5 mM glucose and treated with 1 microM isoproterenol decreased significantly to 0.71+/-0.06 of baseline (n=4; mean+/-SEM). However, permeability did not change in parallel cell columns made from microcarriers cultured in 25 mM glucose (0.97+/-0.2 of baseline permeability; n=4; mean+/-SEM). CONCLUSIONS: High-glucose ***culture*** decreases the retinal endothelial barrier and blocks the response to beta-adrenergic receptors. This model may prove valuable in exploring other hypotheses of increased permeability associated with diabetic retinopathy or other retinal diseases that break down the retinal vascular barrier.

L14 ANSWER 9 OF 132 MEDLINE on STN
ACCESSION NUMBER: 1998293870 MEDLINE
DOCUMENT NUMBER: 98293870 PubMed ID: 9632109
TITLE: Transforming growth factor-beta1 induces apoptotic cell death in cultured ***retinal*** ***endothelial*** ***cells*** but not pericytes: association with decreased expression of p21waf1/cip1.
AUTHOR: Yan Q; Sage E H
CORPORATE SOURCE: Department of Biological Structure, University of Washington, Seattle 98195-7420, USA.
CONTRACT NUMBER: EY04536 (NEI)
GM40711 (NIGMS)
T32 GM07270 (NIGMS)
+
SOURCE: JOURNAL OF CELLULAR BIOCHEMISTRY, ***(1998 Jul 1)*** 70 (1) 70-83.
Journal code: 8205768. ISSN: 0730-2312.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 19980820
Last Updated on STN: 19980820
Entered Medline: 19980812

AB Transforming growth factor-beta1 (TGF-beta1) regulates a variety of cellular functions. In several types of cells, for example, it acts as a growth inhibitor and an inducer of apoptotic cell death. Although one of the important modulators in retinal vascular development and retinal neovascularization, the effects of TGF-beta1 on retinal microvascular cells are not fully defined. We have found that proliferation of both bovine ***retinal*** ***endothelial*** ***cells*** (EC) and pericytes was inhibited by TGF-beta1 in a concentration-dependent manner. However, only retinal EC lost viability after exposure to increasing concentrations of TGF-beta1 (up to 10 microg/ml) in the presence of 2% fetal bovine serum. Dying EC exhibited the morphological and biochemical characteristics of apoptosis. Fragmented nuclei and chromatin condensation were apparent after staining with the fluorochrome Hoechst 33258 and the reagent ApopTag; moreover, gel electrophoresis of DNA from TGF-beta1-treated EC demonstrated degradation of chromatin into the discrete fragments typically associated with apoptosis. The addition of anti-TGF-beta1 neutralizing antibody abolished the apoptotic cell death induced by TGF-beta1. Because not all the EC in a given ***culture*** died after exposure to TGF-beta1, we separated the apoptosis-sensitive

the expression of several proteins associated with this apoptotic pathway. Apoptosis of EC mediated by TGF-beta1 was associated with a decreased level of the cyclin-dependent kinase inhibitor p21waf1/cip1, compared with that observed in the apoptosis-resistant cells. In contrast, the translation product of the tumor-suppressor gene p53 was increased in the TGF-beta1-treated apoptotic cells. Thus, we propose that p21waf1/cip1 and p53 function in distinct pathways that are protective or permissive, respectively, for the apoptotic signals mediated by TGF-beta1.

L14 ANSWER 10 OF 132 MEDLINE on STN
ACCESSION NUMBER: 1998280537 MEDLINE
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AB PURPOSE: Retinopathy of prematurity (ROP) is a vasoproliferative condition that can result in severe visual impairment and blindness in preterm babies. Two conditions seen very early in radioimmunoassay (ROP) are vasoconstriction and vaso-obliteration. A potent vasoconstrictor secreted by endothelial cells is endothelin-1 (ET-1). Premature birth results in a relative systemic hyperoxia, compared to the in utero oxygen milieu. We tested the hypothesis that hyperoxia increases ET-1 expression as a possible mechanism for vasoconstriction in the retinal vasculature. METHODS: Bovine ***retinal*** ***endothelial*** ***cells*** and adrenal capillary endothelial cells were isolated and maintained in ***culture*** . Cells were exposed to control or hyperoxic ***culture*** conditions for 24 h, with and without addition of captopril and nifedipine. Media was collected and assayed for ET-1 by ROP. In addition, cell counts and secreted LDH assays were performed. RESULTS: Conditioned media from cultured bovine retinal and adrenal endothelial cells exposed to hyperoxic ***culture*** conditions for 24 h were found to have higher levels of ET-1 than conditioned media from normoxic control cells. Captopril (10(-6) M and 10(-4) M) and nifedipine (10(-6) M and 10(-4) M) inhibited ET-1 release from hyperoxia-exposed endothelial cells. Under normoxic conditions, ET-1 release was inhibited by 10(-4) M captopril or 10(-4) M nifedipine. CONCLUSIONS: These results demonstrate that (1) hyperoxia stimulates in vitro ET-1 secretion in bovine retinal and adrenal capillary endothelial cells, and (2) captopril and nifedipine downregulate ET-1 secretion under normoxic and hyperoxic ***culture*** conditions, in a dose-dependent fashion. We speculate that ET-1 may be involved in retinal vessel vasoconstriction seen early in the development of ROP. Further, ACE inhibitors and calcium-channel blocking agents, such as captopril and nifedipine, may provide an avenue for blocking vasoconstriction in ROP.

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